AUG 11 1924

Medical Library

VOLUME 28 NUMBER 2

AMERICAN JOURNAL

OF

DISEASES OF CHILDREN

EDITORIAL BOARD

CLIFFORD G. GRULEE, Chicago

OSCAR M. SCHLOSS, New York City — W. McKIM MARRIOTT, St. Louis

FRITZ B. TALBOT, Boston — JOHN HOWLAND, Baltimore

H. F. HELMHOLZ, Rochester, Minn.

AUGUST, 1924

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $4.00

Entered as Second-Class Matter, January 4, 1911, at the Postoffice at Chicago, Illinois, Under Act of Congress of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized on June 14, 1918.

CONTENTS OF PREVIOUS NUMBERS

JUNE, 1924. NUMBER 6

Studies in Growth. 1. Growth of Normal Children. Fritz B. Talbot, M.D., Boston.
Logarithmic Charts in Pediatrics. Carl G. Leo-Wolf, M.D., Niagara Falls, N. Y.
Report of a Case of Gangrene of Legs Following Bronchopneumonia. H. P. Harrell, M.D., Augusta, Ga.
Postencephalitic Behavior Disturbance Without Physical Signs. Bert I. Beverly, M.D., and Mandel Sherman, M.D., Chicago.
A Comparison of the Metabolism of Some Mineral Constituents of Cow's Milk and of Breast Milk in the Same Infant. Chi Che Wang, Ph.D., and Lloyd H. Davis, M.D., Chicago.
The Effect of Fluid on the Temperature and Blood Concentration in the New-Born with Fever. H. Bakwin, M.D.; R. M. Morris, M.D., New York, and J. D. Southworth, M.D., Japan.
The Skin Lesion in Meningococcus Septicemia. C. L. Brown, M.D., Boston.
Tuberculous Pulmonary Cavities in Infancy. David M. Siperstein, M.D., and Harry Baugness, M.D., Minneapolis.
Report of Case of Ectopia Cordis. S. A. Cosgrove, M.D., and A. V. St. George, M.D., New York.
Cerebrospinal Meningitis with Purulent Iridochoroiditis with Recovery. Stafford McLean, M.D., and H. A. Gilmartin, M.D., New York.
Pyloric Hypertrophy in Hypertrophic Pyloric Stenosis. Louis W. Sauer, M.D., Evanston, Ill.
Progress in Pediatrics. Review of the Literature for 1923 on Infant Feeding. Rudolph Duryea Moffett, M.D., New York.
News and Comment.
Abstracts from Current Literature.
Book Review.
Society Transactions:
Chicago Pediatric Society.
Index.

JULY, 1924. NUMBER 1

Causes and Treatment of Otitis Media. 1. Observations on Two Hundred and Five Cases Occurring in Six Hundred and Thirteen Consecutive Hospital Admissions. David T. Smith, M.D., Baltimore.
The Effect of Fasting on the Metabolism of Epileptic Children. Gerald Hoeffel, M.D., and Margaret Moriarity, S.B., Boston.
The Electrocardiogram in Cretinism and in Mongolian Idiocy. Catharine Thacher, Boston.
The Ketogenic Diet in the Treatment of Epilepsy. A Preliminary Report. M. G. Peterman, M.D., Rochester, Minn.
Report of a Case of Streptococcic Meningitis Treated with Injections of Gentian Violet. Lawrence T. Royster, M.D., Charlottesville, Va.
Bone Lesions of Congenital Syphilis. Clifton R. Scott, M.D., New Haven, Conn.
Dermatitis Diphtheritica. Report of Case. Sigmund S. Greenbaum, M.D., Philadelphia.
Roentgen-Ray Studies of Stomach Function. Julian L. Rogatz, M.D., New York.
Roentgen-Ray Studies of Stomach Function: The Peristolic Function. Julian L. Rogatz, M.D., New York.
Acute Appendicitis and Pneumonia in a Baby Fourteen Months of Age. J. Victor Greenebaum, M.D., and J. Louis Ransohoff, M.D., Cincinnati.
Respiratory Diseases in Children: A Review of the Literature from July, 1921, to July, 1923. H. Olding Foucar, M.D., Rochester, Minn.
Abstracts from Current Literature.
News and Comments.
Book Reviews.
Society Transactions:
Saint Louis Pediatric Society.
Chicago Pediatric Society.

COPYRIGHT, 1924, BY THE AMERICAN MEDICAL ASSOCIATION

American Journal of Diseases of Children

VOL. 28 AUGUST, 1924 NO. 2

REFLECTIONS ON CONGENITAL SYPHILIS*

LEONARD FINDLAY, M.D.
GLASGOW, SCOTLAND

I have selected the subject of congenital syphilis for my contribution to the proceedings of your society, in part in deference to the admiration which I have for the vast amount of work, and I should say pioneer work, which America has done, both in the clinical and sociologic fields, and in part because of the peculiar opportunities which I have had of studying the disease. My introduction to the question of congenital syphilis occurred, as I realize only too well, at a most opportune time, synchronizing as it did with the discovery of the Wassermann test and the introduction of arsphenamin. Thanks to Prof. Robert Muir and his work on the problems of immunity, and to his disciple, Carl Browning, who had been a student of Ehrlich, we in Glasgow were ready to appreciate the importance of these great advances in syphilology and anxious to test their value.

THE INCIDENCE OF CONGENITAL SYPHILIS

Though personally I have devoted particular attention to the subject of congenital syphilis I feel that within recent years it has acquired an undue importance, not only in the lay but also in the medical mind. This has undoubtedly resulted from the false ideas which are current regarding its frequency and the part which it plays in infantile mortality and disease. To my mind the importance of congenital syphilis lies not in its frequency, but in the fact that we have at our disposal the means for its almost complete eradication.

The incidence of congenital syphilis has, I think, been grossly exaggerated in many quarters. We in Glasgow have so erred, and I am grateful for the opportunity to correct our early misconceptions. Though I was not responsible for carrying out the tests on the strength of which these early conclusions were based, I supplied much of the clinical material, and thus feel personally reprehensible to a certain extent. Some pediatricians may remember that the opinion which emanated from Glasgow credited 10 per cent. of the infant and child population with being affected with the disease. This figure at the time

* Received for publication, June 26, 1924.
* Read before the Thirty-Sixth Annual Meeting of the American Pediatric Society, Pittsfield, Mass., June 5-7, 1924.

obtained a certain measure of probability, since similar investigations in the field of acquired syphilis revealed an identical percentage incidence.

As time passed, however, some of us came to be rather skeptical of the probability of these estimates, and determined to review afresh the whole question. We were only too conscious of the different estimates, not only for some other districts in our own country, but also of those published for the white population of America.

Naturally a point of paramount importance in the discussion of the incidence of congenital syphilis is the grounds on which a diagnosis of the disease is based. In my opinion the most delicate and reliable test for determining the presence of congenital syphilis is a positive Wassermann reaction. Though the Wassermann test has not introduced us to any manifestations of the disease unknown to the careful observers of the past, it has undoubtedly been of enormous help in the recognition of the individual example of the infection. When properly carried out, I have the utmost confidence in the Wassermann test, and, so far as I can judge from the work of Browning and his colleagues, it cannot as yet be set aside, as some of the recent writers would insist, in favor of the more easily performed Sachs-Georgi reaction. To the foregoing dictum there is, however, one proviso. A positive Wassermann reaction in the new-born is no proof that the child is syphilitic. The antibodies, or whatever calls forth the Wassermann reaction, may pass from the mother to the infant, but it is the spirochetes which cause the disease, and unless spirochetes are present and fresh antibodies formed, the antibodies which emanated from the mother will gradually be eliminated and the child's serum react negatively. I have observed several cases in which the Wassermann reaction was positive during the first month and which in the course of some weeks became negative, without the development of any clinical manifestations of the disease.

In order to show cause for this faith it may be wise to recall an analysis, previously published, which I made of over 1,000 Wassermann reactions, performed for me by Dr. R. M. Buchanan, bacteriologist to the health department of Glasgow. Dr. Buchanan used at that time the original Wassermann technic, and reported as positive all serums which deviated more than four minimal hemolytic doses of complement. From the series of cases investigated I selected all in which the question of early congenital syphilis had arisen, and from the clinical notes made at the time of the first examination, classified them into four groups thus: (1) definite syphilis; (2) ? positive syphilis; (3) ? negative syphilis, and (4) definitely not syphilis.

The first and last groups are self explanatory. The second and third groups comprised cases in which some doubt existed regarding the diagnosis; in the former there was a bias in favor of syphilis and in the latter a bias against syphilis. Table 1 gives the details of the Wassermann tests.

TABLE 1.—*Results of Wassermann Test in Children With Questionable and Unquestionable Syphilis*

Case	Nature of Lesion	Wassermann Reaction +	Wassermann Reaction −	Percentage with + Wassermann Reaction
1	Def. congenital syphilis	161	2	98
2	? positive congenital syphilis	31	10	75
3	? negative congenital syphilis	11	40	21
4	Definitely not syphilis	0	58	0

These findings obtain remarkable confirmation in the results quoted in Table 2, which were obtained with the serums of the mothers of definitely syphilitic and definitely nonsyphilitic children.

TABLE 2.—*Result of the Wassermann Test in Mothers of Syphilitic and Nonsyphilitic Children*

	Wassermann Reaction +	Wassermann Reaction −	Percentage with + Wassermann Reaction
Motheres of syphilitic infants	76	10	88
Mothers of nonsyphilitic infants	0	17	0

It is on the strength then of the Wassermann test that I intend to arrive at an estimate of the incidence of congenital syphilis in Glasgow.

It must be realized that though we speak of the incidence of congenital syphilis in any community we can only arrive at an estimate of its prevalence. It is quite impossible, at least with us in Britain, to obtain an exact measure of its frequency. Such could only be obtained by the study of an average sample of the infant and child population embracing all classes of society. This, of course, is out with practical politics, and we have therefore to fall back on the hospital population, which, it must be appreciated when forming an estimate, is a sick population and hence likely to contain a higher proportion of syphilitic members, and further, what is just as important, a population of one class of society. Any figures from such a study will represent the maximum incidence, even for that particular social class, the actual incidence being undoubtedly considerably less. So long as we bear these points in mind surveys of a large number of children, however, have a very real value.

Working under the egis of the Medical Research Council, we in Glasgow, during the last eighteen months, have carried out a fairly extensive investigation on this question. All children admitted to the Medical Department of the Children's Hospital have been submitted to the Wassermann test. Appreciating, however, as before mentioned, that the patients in this institution are recruited from the poorest section of the community, an attempt was made to rectify this defect by the examination during the same period of all cases of scarlet fever admitted to two wards in the City Isolation Hospital. Cases of scarlet fever were

selected, as all patients with this disease, except perhaps those occurring among the very wealthiest families, are treated in the City Hospital. As the majority, 60 per cent., of the patients in the Children's Hospital are under 3 years of age it was felt that the series of scarlet fever patients would have a further value, as they usually are over 5 or 6 years of age. Dr. W. M. Elliott of Ruchill Fever Hospital was responsible for carrying out the Wassermann tests.

Table 3 gives the details of the results to date.

The points worthy of comment in Table 3 are the small proportion of cases which react positively to the Wassermann test, especially in the case of the scarlet fever patients, and the large proportion of frank syphilis occurring among those giving a positive Wassermann reaction admitted to the Children's Hospital.

I should like to refer, in this connection, to the results obtained within the last few years by Dr. Cruickshank at the Glasgow Maternity Hospital, and which have recently been published as a Green Report by the Medical Research Council (Special Report Series, No. 82).

TABLE 3.—*Results of Wassermann Test on Scarlet Fever Patients*

Source	No. of Cases	Number with + Wassermann Reaction	Number with ? + Wassermann Reaction	Percentage with + Wassermann Reaction	Remarks
Sick Children's Hospital	1,275	38	20	4.5	20% of cases with + Wassermann reaction; frank syphilis
Scarlet fever patients (Ruchill Hospital)	247	1	1	0.8	

Cruickshank performed the Wassermann test, using Harrison's technic, in 1,881 unselected mothers admitted to the Maternity Hospital, and obtained a positive result in 9.04 per cent. of the cases. But not all of the infants born of these syphilitic mothers presented serologic or clinical evidence of the disease. In 1,350 new-born infants examination of the placental blood gave a positive Wassermann reaction in only 4.2 per cent., and even this percentage, in view of what I have already remarked regarding the value of a positive Wassermann reaction in the new-born child, is an overestimate. Cruickshank is also skeptical of the value of the Wassermann test in the new-born, and his experience of the after history of a certain number of these children is worthy of note. He selected for continued observation all those giving a positive Wassermann reaction and in addition a certain number who reacted negatively. In eighty-five of the children followed, the Wassermann reaction remained negative for periods of from ten to twenty months, as it had been at birth; in forty-four children in whom the Wassermann reaction was positive at birth it had become negative within periods varying between three weeks and twenty months: in four cases the positive

Wassermann reaction found at birth persisted up to a period of nineteen months. Thus, only 0.3 per cent. of children born in the Maternity Hospital could be considered syphilitic, and Cruickshank concluded that the incidence of congenital syphilis amounted to considerably under 1 per cent. of the infant and child population.

It must be admitted that the above periods of continued observation are not very prolonged, and one must therefore guard against dogmatism on the question. There undoubtedly remains the possibility of the development later by a positive Wassermann reaction or of symptoms in the form of syphilis hereditaria tarda. I have been fortunate in having the opportunity of following up children in whom there was the possibility of the infection having existed in such a latent form for as many as ten years, but have never seen any active manifestations of the disease develop. In two children, however, in whom there had been earlier a negative Wassermann reaction, there appeared at 5 and 7 years, respectively, a weak positive reaction of the serum. The serum of the child who reacted positively at 7 years gave a definitely negative result when retested at 9½ years. In view of these results then one can only conclude that a child who reacts negatively at birth may develop a weak positive Wassermann reaction at a later date and thus possibly suffer from syphilis tarda. Though this contingency is unlikely, there would consequently seem to be some justification for the practice of Adam in treating all children of syphilitic mothers after birth, and not only those who react positively.

Nevertheless, such examples of syphilis tarda will probably be few and thus our latest work on the incidence of congenital syphilis is more in accordance with the ideas of its prevalence entertained by the purely clinical observers, e. g., Still [1] and also with the estimates of Williams, Jeans and Holt for the white population of America, than with the notorious early Glasgow figures. I consider with Cruckshank that in Glasgow something under, and probably considerably under, 1 per cent. of the infant and child population is infected with the *Spirocheta pallida*.

THE MANIFESTATIONS OF CONGENITAL SYPHILIS

It is remarkable what little help we have gained from the modern methods of diagnosis in the recognition of the manifestations of syphilis. I think it can truly be said that the Wassermann reaction has not disclosed to us any one evidence of congenital syphilis, with the possible exception of eczema oris syphiliticum, which was unknown to our predecessors.

I recall some remarks made by Sir Humphrey Rolleston, in a most philosophical introduction to a discussion on congenital syphilis before

1. Still: Common Diseases of Infancy and Childhood, London, Oxford Univ. Press, 1915, p. 792.

the Royal Society of Medicine. In the course of his remarks Sir Humphrey raised the question of all varieties of endocrine disease, anemia, mitral stenosis and rickets being of syphilitic or parasyphilitic origin, using the latter term in its true etymologic sense. Until we discover, however, a more delicate evidence of the presence of the disease than the Wassermann reaction, discussion of such a problem can be no more than hypothetical in nature and can lead us to no definite conclusions.

In the pre-Wassermann days many of our predecessors taught that general paralysis, tabes, aortic aneurysm, and paroxysmal hemoglobinuria were invariably syphilitic, or what they called parasyphilitic, in nature. It was also generally taught in those pre-Wassermann days that mental deficiency, epilepsy, congenital heart disease and hepatic cirrhosis, as well as many other conditions, might occasionally be due to the treponema pallida. In fact, syphilis has long been looked on as the great imitator of other diseases. Was it not this fact which prompted Sir William Osler to say before the British Royal Commission on Venereal Disease that he could "teach all medicine on syphilis"?

With the advent of the Wassermann test it was natural that this very question should be tackled from the serologic angle. We know how the opinions of our predecessors, the good old clinicians of the past, have been wholly confirmed and we are left with wonder at their clinical acumen. One of course would not have been surprised to find that a delicate serologic test like the complement deviation test would disclose syphilis where it had not been suspected on clinical grounds, and certainly the earlier records did not disappoint us. In my own school extensive investigations of this nature were undertaken, and in consequence of the findings Glasgow earned for itself at the time the reputation of being the most syphilitic city in Britain. Watson, Fraser and Chislett, as a result of their work, considered that the purely clinical observers had very much underestimated the rôle that syphilis plays in mental deficiency, epilepsy, spastic diplegia and congenital heart disease. Instead of the 1 to 2 per cent. of the clinicians they concluded that syphilis was responsible for from 50 to 60 per cent. of these diseased conditions. In this same connection I may also refer to the work of Steevens [2] on mongolian idiocy, and the idea current in many child-welfare centers even today that marasmus or malnutrition in infancy is frequently due to syphilis.

At the time of the reports of Watson and his co-workers I considered the case proved that syphilis was a most important factor in the causation of the foregoing maladies, but more extended and personal investigation has shaken my faith in their value. It has always seemed

2. Steevens: Am. J. Obst. **75**:36, 1917.

to me remarkable that in this field alone of all syphilitic manifestations there should be such discrepancies between the ideas of our teachers and those of ourselves.

In Table 4 are synopsised the findings in a series of diseases, some of which we know are occasionally syphilitic in origin and others again the cause of which is entirely unknown. In order to enhance the value of these results they have been given in two series; the first refers to cases investigated between 1914 and 1922 and the second series is abstracted from the findings by Dr. Elliott in the investigation at present in progress to gain an idea of the incidence of congenital syphilis.

The points worthy of note in Table 4 are (1) the regular presence of a positive Wassermann reaction in frank syphilis or syphilitic conditions, (2) the occasional finding of a positive Wassermann reaction in

TABLE 4.—*Result of the Wassermann Test in Various Diseases*

	Wassermann Reaction			
	First Series		Second Series	
	+	−	+	−
Mental deficiency	4	37	1	23
Mongolian idiocy	1	6	0	4
Hydrocephalus	4	37	0	8
Epilepsy	1	9	0	20
Convulsions	..	..	0	22
Lateral sclerosis	2	0	1	0
Cerebral tumor	1	14	0	16
Spastic diplegia	1	17	1	8
Encephalitis (not lethargic)	0	12	1	9
Encephalitis (lethargic)	..	..	0	11
Obliteration of bile ducts	0	9	0	2
Pyloric stenosis	..	..	0	16
Von Jaksch's anemia	2	18	0	7
Congenital heart disease	0	13	0	4
Marasmus	1	13	2	110
Nephritis	..	..	0	71
Congenital syphilis	..	..	8	0

diseases which we know have sometimes a syphilitic basis, and (3) the almost invariable absence of a positive Wassermann reaction in diseases which we have clinically never felt justified in classifying as syphilitic in nature. The findings as a whole substantiate the opinions come to by the clinical observers of the past and are a complete refutation of the early views of the Glasgow school.

A discussion of the various manifestations of congenital syphilis would be incomplete without a mention of the possibility of different varieties of the *Spirocheta pallida* being responsible for different types of the disease. That there is a special neurotropic variety of the organism has been debated for many years. The now well known and often recorded instances, observed by Babinski, Marie, Erb, Morel-Lavallee, Mott and Brosius, of several persons infected from the same source developing neurosyphilis later make such a possibility not unlikely. Congenital syphilis would seem to be a wide field in which to get

evidence on this interesting question, as here we have whole groups of persons, a whole family, undoubtedly infected with the one organism. One, however, must not forget in this connection the influence of family predisposition, which of course would tend rather to increase than minimize any evidence in favor of a special type of toxin. Thomson [3] recorded about twenty-six years ago a series of syphilitic families in which there was a marked tendency to implication of the same tissues.

I have had the opportunity of observing in all, twenty cases of neurosyphilis, but in only three instances was there a history of anything suggesting neurosyphilis in any other member of the family, parents or children, although the mother in all cases and several children in not a few of the families reacted positively to the Wassermann test. There had occurred in the above families a total of 119 pregnancies, 106 of which resulted in the birth of a living child. In three of the families one other child had died of meningitis, which in one instance was most probably tubercular in nature as it was associated with morbus coxae, and in another family one child had suffered from convulsions. Otherwise as previously mentioned there was no history or evidence of nervous disease in the family.

One striking feature in all the families in which examples of neurosyphilis occurred was the good, or at least reputed good health of the other members living. The proportion of living members, too, was distinctly higher than that which is usually met with in syphilitic families. In these twenty families 57 per cent. of the 119 children were still alive at the time of examination, whereas in twenty-one syphilitic families referred to later only 31 per cent. of ninety possible children were living. It is remarkable, too, that in only three of the twenty patients was there a history of rash or snuffles obtained, or anything suggesting early manifestations of the disease, though in one of the above cases there was a typical saddle nose and in still another scarring around the mouth definitely pointing to the presence of early syphilis. In short, neurosyphilis seemed to occur in the family not severely infected, although of course instances were met with in which definite stigmas, in the form of choroiditis, scarring around the mouth, Hutchinsonian teeth and a positive Wassermann reaction were obtained in other members of the family.

This evidence, therefore, so far as it goes is distinctly against the idea of a special neurotropic toxin but tends rather to confirm the view expressed by Mott that neurosyphilis is more an evidence of an attenuated toxin. Mott in an analysis of his cases of juvenile general paralysis showed that it tended to occur in the later members of the family after a series of miscarriages, stillbirths and deaths in early

3. Thomson, J.: The Scottish Medical and Surgical Journal, 1898.

infancy. He also stated that he had found it exceedingly difficult to infect animals with the brain tissue of patients with general paralysis, although it was rich in spirochetes. On these grounds then, one would have expected infection of the nervous system to be unduly frequent in the congenital variety of the disease, as its low infectivity undoubtedly points to an attenuation of the toxin. I know that Jeans has recently recorded that the cerebrospinal fluid in congenital syphilis frequently reacts positively to the Wassermann test, but although I have no definite figures to quote on the point, I am inclined to believe from general impressions that the proportion of neurosyphilis is much less in the congenital than in the acquired variety of the disease. This, of course, will be in part accounted for by the high mortality in its early stages.

However, the result of any infection depends not only on the virulence of the infecting agent but also on the resistance of the host and can be represented by the equation, symptom complex = R. The absence of any family predisposition to neurosyphilis would tempt us to eliminate from the argument the question of the host, but the experience that general paralysis rarely occurs in persons who are infected with malaria, or who have suffered from a febrile illness shortly after acquiring syphilis, would suggest that after all the host may play a not unimportant part in the development or otherwise of neurosyphilis.

THE TREATMENT OF CONGENITAL SYPHILIS

The treatment of congenital syphilis can be divided into curative and prophylactic, and in my opinion the curative type of treatment is a failure. No doubt, with the newer preparations, the disease is not so dangerous to life as in the prearsphenamin days, and many children are now saved who previously would have died, but a cure, at least in the sense in which we understand it today, is unfortunately obtained in only a minority of cases. By a cure I take it we mean a disappearance of all symptoms and a persistently negative Wassermann reaction. This inability to cure is specially marked in the case of the late manifestations of the disease in the older children. My colleagues and I have frequently referred to this point, and in Table 5 our experience during successive years is summarized.

It is interesting to note in Table 5 that in addition to the frequency with which the negative Wassermann reaction again became positive, especially in children over 1 year of age, there has been a decline in the percentage of primary cures. In the series of cases treated in 1922 often as many as twenty-eight injections had to be given to effect a cure. This we are inclined to ascribe to the inferiority of the preparations supplied during the later years.

These results contrast markedly with those obtained by the prophylactic method, i. e., treatment of the pregnant mother. There have now been treated at the venereal clinic of the hospital some fifty pregnant syphilitic mothers, and in all except three a living and apparently nonsyphilitic child was obtained. In one case a definitely syphilitic child was born, but in this instance treatment of the mother was only instituted during the last two weeks of the pregnancy. In the other two cases the children were stillborn, apparently the result of a difficult labor; in neither instance was there any definite evidence of syphilis. In several of the living and apparently healthy babies the Wassermann reaction was positive at birth, but in the course of some weeks this became negative, and I am inclined to ascribe the positive reaction not to the presence of spirochetes but to antibodies which have passed over from the mother. In all these cases the serum of the mother at the date

TABLE 5.—*Result of Curative Treatment During Successive Years in Glasgow*

Year	Author	No. of Cases	Age	Result
1920	Findlay	31	Under 3 months	75% cures after course of from 7 to 10 injections; no relapses within from 6 to 12 months
1921	Fleming	47	Under 1 year	98% primary cures but in 30% of those retested 6 months to 4 years later Wassermann reaction again positive
	Fleming	27	Over 1 year	78% primary cures but in 43% of those retested Wassermann reaction again positive
1922	Galbraith	25	Under 1 year	84% primary cures after course of treatment consisting of from 7 to 28 injections; fourteen examined 4 to 12 months later with no relapses
	Galbraith	18	Over 1 year	30% primary cures after course of treatment consisting of from 7 to 28 injections; two recovered within 6 months and both relapsed

of birth reacted positively to the Wassermann test. In not one of the cases which have been followed has any clinical evidence of syphilis declared itself, but that such may arise later is possible in view of the development referred to in the foregoing of a weak positive serologic reaction in some of the children which have been longest under observation.

These results of the prophylactic method of treatment are quite comparable with those recorded by all workers in this field. I have treated mothers from all periods of pregnancy, and found that so long as treatment was commenced before the eighth month success was attained. I have given as few as four injections each of 0.6 gm. of neoarsphenamin, and as many as forty-two without seeing any difference in the result.

One very important point in this method of treatment is that not only are all children born alive apparently free from the disease but all miscarriages and stillbirths are avoided. The great saving in life

by prophylaxis is well seen by Table 6, in which the result of conceptions before and after prophylactic treatment are contrasted in twenty-one families.

A striking feature in this form of treatment is that a healthy non-syphilitic child may be born even although the mother's serum continues to react positively to the Wassermann test. This suggests to me that, as Neisser taught, the source of the disease in the fetus is the fetal and maternal decidua, which on account of its extreme vascularity gives easy access to the spirocheticide circulating in the blood. It would seem, too, that so long as the disease in this region is eradicated no harm can come to the fetus. A focus locked up in the brain or a bone, and surrounded by fibrous tissue, will be of as little danger to the fetus as it is beyond the reach of the drug. Antibodies may, however, continue to be manufactured and cause the mother's serum to react positively. This line of thought immediately calls to our mind a possible

TABLE 6.—*Result of Prophylactic Treatment*

	Number		
21 Families	Living	Dead	Syphilitic
Fate of pregnancy before treatment.....	28	34 (69%)	28 = 31%
Fate of pregnancy after treatment.....	34	1* (10.5%)	3† = 8%

* Difficult labor.
† No active symptoms, but Wassermann reaction positive at one month only.

explanation of the ineffectiveness of any antisyphilitic treatment of interstitial keratitis. The sclera is an extremely avascular structure; in fetal life and very early life, however, it is more vascular and may at this time permit the entrance of the spirochete, but for some unknown reason it would seem to lie dormant in the sclera until later on in life it makes itself evident. But this evidence only occurs when the structure is for all practical purposes hermetically sealed, and thus defies admission to the body fluids. I can recall the case of a child that I saw at the age of 4 months with severe congenital syphilis. By means of heroic treatment with mercury and arsphenamin all symptoms disappeared, and a negative Wassermann reaction was obtained. I was able to keep this child under observation and had the serum tested repeatedly but always with a negative result, yet at the age of 7 years, when the Wassermann reaction was still negative, severe interstitial keratitis appeared. I have no doubt that it is cases such as this and the absence of all response to specific treatment which have suggested that the tubercle bacillus may play a rôle in keratitis.

Yet another and more salutary result of antenatal treatment of congenital syphilis is the way in which these syphilitic women continue to give birth to healthy nonsyphilitic children without the institution of another course. I thought previously that this was the invariable rule, but more extended experience has taught me that though none of the children have ever presented any symptoms, their serums may very occasionally react faintly positively to the Wassermann test and thus they must be considered latent syphilitic patients. This, however, I consider a rare event. I have had the opportunity of keeping under observation four families in which there have been from four to six pregnancies since the mothers were treated, and I have been permitted to examine and test the children periodically. In view of the interest of these clinical records I append them in summary form.

REPORT OF CASES

CASE 1.—Mrs. M., has had five previous pregnancies; there were no miscarriages; the fifth child was definitely syphilitic. The Wassermann reaction was positive in the mother and child. The fourth child at 17 years of age had a doubtful positive reaction.

On Feb. 21, 1914, the patient was seven months pregnant. Mercurial inunction was commenced. From February 22 until March 22, four injections (three of 0.6 and one of 0.9 gm.) of neo-arsphenamin were given. April 7, the Wassermann reaction was still positive, but weak. There was no further treatment.

April 25, the sixth child, a girl, was born. June 22, at 8 weeks, the Wassermann reaction was negative. March 8, 1915, at 11 months the Wassermann reaction was negative. At 4½ years the reaction was negative. At 7 years the reaction was negative, and April 24, 1924, at 10 years, the reaction was still negative, the child being well all along.

Sept. 1, 1916, the seventh child, a boy, was born. Up to April 13, 1924, the Wassermann reaction was negative.

Feb. 10, 1921, the mother's Wassermann reaction was negative.

In 1921, the eighth child, a girl, was born, and at the age of 2½ years the Wassermann reaction was still negative.

In 1924, the ninth child, a boy, was born, he was always well. April 13, at 5 months, the Wassermann reaction was negative.

CASE 2.—Mrs. K., has had three previous pregnancies; the first child had a rash on its body and died at 2 months; the second child, born in the eighth month of pregnancy, only lived one month; the third child seen by me was typically syphilitic and died at 2 months. The mother's serum at this time reacted positively to the Wassermann test.

April 22, 1914, the patient was two months pregnant. Mercurial inunction was commenced, and from April 24 till July 1, five injections of 0.6 gm. neo-arsphenamin were given. There was no treatment of the mother since.

November 2, the fourth child, a boy, was born. At 4 months the Wassermann reaction was negative, and remained so until April 16, 1924. The child has always been well.

Jan. 7, 1917, the fifth child, a girl, was born. On April 16, 1924, the Wassermann reaction was negative. The child has always been well.

April 9, 1919, the sixth child, a boy, was born. At 2½ years the Wassermann reaction was negative. At 5 years the Wassermann reaction ? positive (doubtful). The child has always been well.

June 8, 1921, the mother's Wassermann reaction was positive.

August, 1921, the seventh child, a girl, was born. April 16, 1924, at 2 years and 9 months, the Wassermann reaction was positive. The child has always been well.

August, 1923, the eighth child, a girl, was born. At 8 months the Wassermann reaction was negative. The child has always been well.

CASE 3.—Mrs. S., has had seven previous pregnancies. The last child was typically syphilitic and gave a positive Wassermann reaction.

April 22, 1914, the patient was two months pregnant. The Wassermann reaction was positive, and mercurial inunctions were commenced and continued until July 1. Five injections of 0.6 gm. each of neoarsphenamin were given. June 8, the Wassermann reaction was negative.

October 12, the eighth child, a boy, was born. There was no treatment of the mother since. At 3 months the Wassermann reaction was negative. At 7 years the Wassermann reaction ? positive (weak). At 9 years the Wassermann reaction was negative. The child has always been well.

Jan. 15, 1916, the ninth child, a boy, was stillborn, after a difficult labor.

Jan. 5, 1917, the tenth child, a girl, was born. At 4½ years, the Wassermann reaction was doubtful. At 7¼ years, the Wassermann reaction was negative.

May 15, 1919, the eleventh child, a boy, was born. June 21, 1921, at the age of 2 years, the Wassermann reaction was negative. April 13, 1924, the Wassermann reaction was negative.

Dec. 16, 1920, the twelfth child, a girl, was born. At 6 months, the Wassermann reaction was negative. April 13, 1924, the Wassermann reaction was negative.

June 21, 1921, the mother's Wassermann reaction was negative.

CASE 4.—Mrs. McN., has had four previous pregnancies; the first child died at 10 months from bronchitis; the second died at 8 months; the third is alive, syphilitic stigmata and positive Wassermann reaction; the fourth, seen by me, at the age of 13 months, had severe congenital syphilis.

Sept. 30, 1914, the patient was seven months pregnant. The Wassermann reaction was positive. Mercurial inunction was commenced, and lasted until October 10. Four injections of 0.6 gm. neoarsphenaminin were given.

December 2, the fifth child, a boy, was born. At 3 months, the Wassermann reaction was negative. The child died at the age of 4 months of bronchopneumonia.

Jan. 24, 1916, the sixth child, a girl, was born. At 4 months, the Wassermann reaction was negative. The child died, aged 6 months, of bronchopneumonia.

Jan. 12, 1917, the mother's Wassermann reaction was positive.

January 7, the seventh child, a boy, was born. April 13, 1924, at the age of 7 years, the Wassermann reaction was negative. The child has always been well.

Jan. 8, 1918, the mother's Wassermann reaction was negative.

July 29, 1919, the eighth child, a girl, was born. She had no evidence of congenital syphilis. She died, aged 7 weeks, of bronchopneumonia.

Oct. 2, 1920, the ninth child, a boy, was born. There was no evidence of congenital syphilis. He died, aged 2 months, of bronchopneumonia.

June 30, 1921, the mother's Wassermann reaction was negative.

Jan. 22, 1923, the tenth child, a girl, was born. April 13, 1924, the child aged 15 months, had a negative Wassermann reaction. The child has always been well.

CONCLUSION

The only conclusion that I can come to as a result of my experience of the treatment of congenital syphilis is that our hope for its eradication lies in prophylaxis. But that such treatment can be carried out as

extensively as is required necessitates the notification of syphilis, or at least the notification of congenital syphilis, and I sincerely trust that your countrymen will continue as they have in the past to collect evidence on this point, and as missionaries, help in the conversion of my compatriots.

SOME FURTHER OBSERVATIONS ON THE LANGE GOLD CHLORID REACTION ON THE CEREBROSPINAL FLUID IN INFANTS AND YOUNG CHILDREN *

C. G. GRULEE, M.D.
CHICAGO

In 1915, Moody and myself [1] reported on the findings in the cerebrospinal fluid with the Lange colloidal gold reaction. The first of the conclusions in this paper, was: "In the cases of congenital syphilis included in this report the cerebrospinal fluid reacted to the colloidal gold chlorid solution always in the lowered dilutions, and with a marked degree of regularity strongest in the dilutions of 1:40 and 1:80." "There is a small group of cases of congenital syphilis in which the reaction is similar to that of paretic dementia."

In Table 1, I have collected a few cases of congenital syphilis, in which the reactions in general do not conform to the first statement. It will be noted in this table that Case 5 conforms very well to the second statement, and that Case 6 likewise shows a reaction similar to that obtained in paretic dementia. Both of these are cases of syphilitic meningitis. It will be noted further, that in Cases 1, 2, 9, and 10, though the blood Wassermann was positive, the cerebrospinal fluid showed nothing whatever significant, since we may disregard the "1" reaction in such a case. It will also be noted that the same was true once with Cases 11 and 13. In other words, a strong blood Wassermann in these cases was not accompanied by a reaction in the cerebrospinal fluid. It may be noted further, that in Case 6, while the spinal fluid gave a strong reaction, the blood Wassermann was negative.

In the other cases, reaction of the blood and the spinal fluid conformed very well; only, however, in the first test made on Case 4, and in the second on Case 13, they conformed to the rule that most marked reactions occur in the dilutions of 1:40 and 1:80, and it is to be noted that in Case 13, where the cerebrospinal symptoms predominated, the spinal fluid did not give the reaction which might be expected. It should be remembered that the cases herein mentioned are selected cases, but they do not conform in a general way to statements of the

* Received for publication, June 25, 1924.

* Read before the Thirty-Sixth Annual Meeting of the American Pediatric Society, Pittsfield, Mass., June 5-7, 1924.

1. Grulee, C. G., and Moody, A. M.: The Lange Gold Chlorid Reaction on the Cerebrospinal Fluid of Infants and Young Children, Am. J. Dis. Child. **9**: 17 (Jan.) 1915.

TABLE 1.—*Congenital Syphilis*

Case	Date	Age	Spinal Fluid: Cells	Nonne	Wassermann	Gold Chlorid	Blood Wassermann	Remarks
1	11/ 5/19	13 mo.	4	0	—	0111110000	+++	Congenital syphilis, epilepsy, pyelocystitis
2	11/ 5/19	3 yr.	4	0	—	0111100000	+++	Congential syphilis, epilepsy, suppurative cervical adenitis
3	1/ 9/20	11 wk.	—	++	++++	1123332100	+++	Congenital syphilis
4	3/28/19	19 mo.	6	+	0	0122110000	+++	Congenital syphilis, infantile scurvy, mental deficiency, pyelocystitis
	4/17/19	20 mo.	5	0	0	0111100000	++	
5	5/10/22	4 mo.	99	++	++++	2345554321	—	Syphilitic meningitis
	5/26/22	4½ mo.	76	++	++++	2345554321	—	
6	4/21/22	17 mo.	54	+	+++	1223321100	..	Syphilitic meningitis
7	11/ 7/22	4 mo.	28	+	++++	1223210000	++++	Congenital syphilis
8	2/18/21	6 wk.	16	+	+++	1123210000	++++	Congenital syphilis
9	12/14/21	8 mo.	4	0	0	0111000000	++++	Congenital syphilis
10	1/20/22	18 mo.	4	0	0	0111000000	+++	Congenital syphilis, spasmophilia, cretinism, pyelocystitis, rickets, measles
11	5/23/21	5 mo.	4	0	0	0111000000	++++	Congenital syphilis, syphilitic hydrocephalus, optic atrophy
	6/ 6/21	5½ mo.	30	+	—	3222110000	—	
12	7/ 5/21	5 mo.	6	+	0	0112100000	++++	Congenital syphilis
13	2/ 2/17	17½ mo.	6	0	0	0000000000	—	Congenital syphilis, cerebrospinal
	1/15/19	28½ mo.	2	+	0	0121100000	+++	

TABLE 2.—*Tuberculous Meningitis*

Case	Date	Age	Spinal Fluid: Cells	Nonne	Wassermann	Gold Chlorid	Blood Wassermann
1	7/12/15	3 mo.	10	+	—	1123333110	—
2	2/21/15	13½ yr.	77	++	..	0000123100	..
3	2/14/16	3 yr.	396	++	++	0000121000	..
			148	+++	+	.....	—
4	3/12/19	2½ yr.	200	++	+	0001221000	..
5	4/14/20	4 yr.	30	+	—	0112221100	..
6	6/30/20	7 yr.	280	+	..	0012221100	—
7	1/31/21	2 yr.	54	+	—	0012221000	..
8	5/ 4/23	6 mo.	155	+	..	0000123210	..
9	4/11/23	6 mo.	55	+	—	1122110000	..
	4/23/23	.....	34	+	—	1112210000	..
	4/26/23	.....	14	+	..	0011221000	..
	4/30/23	.....	4	+	..	0001332110	..
10	6/28/23	4 yr.	...	+	—	1112110000	..
	6/11/23	.....	...	+	..	1123210000	..
11	1/23/23	9 yr.	156	+	..	0012100000	..
			Cerebrospinal Meningitis				
12	5/25/14	19 mo.	250	+	0	--1122221-	..
			Streptococcic Meningitis				
13	4/16/21	2 mo.	...	+	..	0000112201	..
			Encephalitis Lethargica				
14	1/ 5/20	2½ yr.	5	+	0	0122100000	..

former thesis and I wish to take note here of the exceptions. It also should be noted that the Wassermann reaction may be negative in the blood, but positive in the spinal fluid.

The second group of cases (Table 2) has to do with tuberculous meningitis. In our previous report, the fourth conclusion was that: "The reaction in tuberculous meningitis is found to be most intense in dilutions of 1:160 and 1:320." It is likely that the more rapid the course, the more apt is the reaction to occur in higher dilutions. The second table, of tuberculous meningitis cases, conforms in general to this rule. It is seen, however, that the reaction varies in different cases. The intensity is by no means always of greatest strength in the fifth and sixth tubes. Rather interesting to note is Case 9, where there was a rapid transition from lower to higher dilutions. If we compare with these two cases the one of cerebrospinal meningitis (Case 12), and the other case of streptococcic meningitis (Case 13), we find that the difference between these reactions and those of tuberculous meningitis is not very distinct in certain instances. In the case of encephalitis lethargica (Case 14), the reaction more nearly approaches that which we commonly expect to find in congenital syphilis.

The series of cases of mental deficiency and idiocy (Table 3), shows that there is rarely a reaction greater than "1" in any of the dilutions and that there is no regularity in the findings. One may suspect, however, that this repeated finding of slight variation in color in so many tubes may have some significance and recognize that it is found very regularly in various cases of idiocy.

Table 4 consists of cases of epilepsy, all but one of them of the idiopathic variety. In only one of these (Case 4) was there any reaction in the spinal fluid higher than a slight variation in color. Unfortunately in this case the blood Wassermann was not done. The Wassermann on the spinal fluid, however, was negative.

CONCLUSIONS

1. In congenital syphilis, the colloidal gold reaction in the spinal fluid may assume at times the same degree as that shown in cases of paretic dementia. In this series, this occurred twice in cases of syphilitic meningitis.

2. Congenital syphilis varies rather frequently from the usual reaction, that is, a fluid which shows the greatest reaction in dilutions of 1:40 and 1:80.

3. There is no regular agreement between the blood Wassermann and the Wassermann and colloidal gold reactions in the spinal fluid.

4. There may be a strong reaction both to the Wassermann and to the colloidal gold solution in the spinal fluid with a negative blood Wassermann.

TABLE 3.—*Mental Deficiency*

Case	Date	Age	Spinal Fluid: Cells	Nonne	Wassermann	Gold Chlorid	Blood Wassermann	Remarks
1	10/ 9/16	4 yr.	1	0	0	0000000000	0	Mental deficiency and Idiocy
2	11/ 2/14	9 mo.	2	0	0	1100000000	..	Feebleminded
3	11/ 2/14	13 mo.	2	0	0	0001110000	0	Idiocy
4	2/25/20	14 mo.	4	0	..	0011100000	0	Idiocy
5	5/17/19	23 mo.	3	0	0	0111000000	0	Idiocy
6	7/16/19	2⅓ mo.	3	+	0	0111100000	..	Mongolian idiocy
7	6/ 9/19	14 mo.	8	0	0	0111000000	0	Idiocy
8	3/20/20	6 yr.	4	0	0	0111100000	..	Mental deficiency
9	6/ 6/19	2½ yr.	5	0	0	0111000000	0	Idiocy
10	6/ 1/17	8 mo.	80	0	0	2211000000	..	Idiocy
11	8/ 9/19	18 mo.	2	0	0	0110000000	0	Mental deficiency
12	1/12/21	13 mo.	3	0	0	0111100000	..	Mental deficiency
13	10/20/22	14 mo.	1	0	0	0110000000	..	
14	4/15/21	3½ yr.	6	+	0	0122110000	0	Mental deficiency and spastic paraplegia
15	6/22/21	30 mo.	3	0	0	0110000000	..	Idiocy
16	10/23/22	18 mo.	..	..	..	0100000000	..	Mongolian idiocy
17	3/ 7/21	6 mo.	7	+	0	0112100000	..	Suspect idiocy
18	3/27/22	5 yr.	5	+	0	0111000000	..	Mental deficiency
19	3/23/21	5 yr.	2	0	0	0111000000	..	Mongolian idiocy, anemia, pseudoleukemia Von Jaksch's
20	10/21/21	14 mo.	5	0	0	0111100000	..	Idiocy and congenital cataract
21	1/ 9/22	8 yr.	2	0	0	0110000000	..	Mental deficiency and epilepsy
22	5/ 8/22	6 mo.	6	+	0	0111100000	..	Mental deficiency
23	5/10/22	6 mo.	4	0	0	0111000000	..	Mental deficiency and convulsions
24	10/ 3/21	19 mo.	2	0	0	0011000000	0	Idiocy
25	4/21/22	8 yr.	4	+	0	0121100000	..	Mongolian idiocy
26	1/10/21	6 mo.	5	0	0	0111100000	..	Suspect idiocy
27	31/ 8/21	9½ mo.	4	0	0	0111000000	..	Idiocy
28	3/21/21	2 yr.	5	0	0	0112110000	0	Suspect idiocy
29	1/17/21	15 mo.	4	0	0	0111100000	..	Idiocy
30	2/ 1/22	20 mo.	3	0	0	0110000000	..	Mental deficiency
31	9/15/22	1 yr.	4	0	0	0111100000	..	Mongolian idiocy
32	4/ 4/21	2½ yr.	4	0	0	0111000000	..	Imbecility and spastic paraplegia
33	6/22/23	2 yr.	0	0	0	1110000000	..	Idiocy micropthalmos
34	6/27/23	17 mo.	0	0	0	0000000000	0	Idiocy
35	7/ 2/23	8 mo.	7	0	?	0110000000	..	Idiocy micropthalmos
36	10/19/23	6½ yr.	1	0	0	0000000000	..	Idiocy
37	5/28/20	5 yr.	4	0	0	0111100000	0	Mental deficiency and epilepsy

TABLE 4.—*Epilepsy*

Case	Date	Age, Years	Spinal Fluid: Cells	Nonne	Wassermann	Gold Chlorid	Blood Wassermann	Remarks
1	6/23/15	2½	1	0	+	0000000000	+	Epilepsy
2	5/ 3/15	4½	3	0	0	0000000000	0	Idiopathic epilepsy
3	9/27/14	4	?	0	?	1100000000	..	Epilepsy
4	7/ 9/20	2	3	0	0	0122211000	..	Epilepsy
5	8/ 3/21	4	3	0	0	0110000000	..	Epilepsy
6	11/24/22	8	?	0	0	0100000000	..	Epilepsy
7	10/25/22	7	3	0	0	1110000000	0	Epilepsy
8	8/ 4/22	9	4	0	0	0111100000	..	Epilepsy
9	1/31/23	9	4	0	0	0110000000	..	Idiopathic epilepsy
10	5/ 9/23	8	0	0	0	0110000000	..	Jacksonian epilepsy
11	6/15/23	8	?	0	0	0110000000	..	Epilepsy, Jacksonian post-encephalitic
12	7/16/23	10	0	0	0	0000000000	..	Epilepsy
13	9/ 7/23	?	5	0	0	0010000000	..	Idiopathic epilepsy
14	10/24/23	..	3	+	0	0111000000	..	Epilepsy

5. Tuberculous meningitis more nearly conforms to the reaction with greatest intensity in dilutions of 1 : 160 and 1 : 320. It may, however, vary considerably from this in certain cases showing a progressive variation as the meningitis extends.

6. Other conditions which clinically may be easily confused with tuberculous meningitis, may show a colloidal gold reaction not dissimilar from that which is seen in certain cases of tuberculous meningitis.

7. There is no definite reaction in most cases of idiocy and epilepsv.

STUDIES IN GROWTH*

III. GROWTH OF UNTREATED MONGOLIAN IDIOTS

FRITZ B. TALBOT, M.D.

BOSTON

This series of untreated mongolian idiots, between the ages of 4 months and 10 years, has been studied from the point of view of growth of different parts of the body. The findings have been plotted to the growth curve of normal children, constructed from a series of body surface measurements taken according to the DuBois linear formula.

In Chart 1 the standing heights of these cases are shown according to age.

These findings show a close proximity up to the first year of life, after which there is a tendency for the mongolian idiot to be shorter than the normal. While this may be said to be due in some cases to the occurrence of rickets, which is frequently seen in this condition, it is by no means the sole explanation, and the retardation of growth is not so pronounced as it is in cretinism.

On the basis of height referred to weight these cases of untreated mongolianism show a closer correlation to the normal; the cases falling very close to the expected weight for height.

Since evidence of malnutrition is frequently met with in cases of untreated mongolian idiots, contrary findings were expected. The apparent discrepancy may be due to the abnormal fat deposits, especially noticeable in the neck, upper part of the back and dorsum of the hands and feet. With the disappearance of this superfluous fat, after thyroid therapy, the ear marks of malnutrition and the disproportion between height and weight are more marked.

On clinical observation these patients obviously seem to have a greater length of trunk than normal patients. These observations, however, were not corroborated by body surface measurements in the majority of instances as shown in Charts 3 and 4.

Measurements of the circumference of the head were taken over the occiput and around the frontal bosses. The contour of the head was abnormal in nearly all instances, despite the fact that in several instances the findings fall within normal limits.

---

* Received for publication, May 21, 1924.

* From the Children's Medical Department, Massachusetts General Hospital. This paper is No. 24 of a series of studies in metabolism from the Harvard Medical School and allied hospitals. The expenses of this investigation have been defrayed in part by a grant from the Proctor Fund of the Harvard Medical School for the study of chronic diseases.

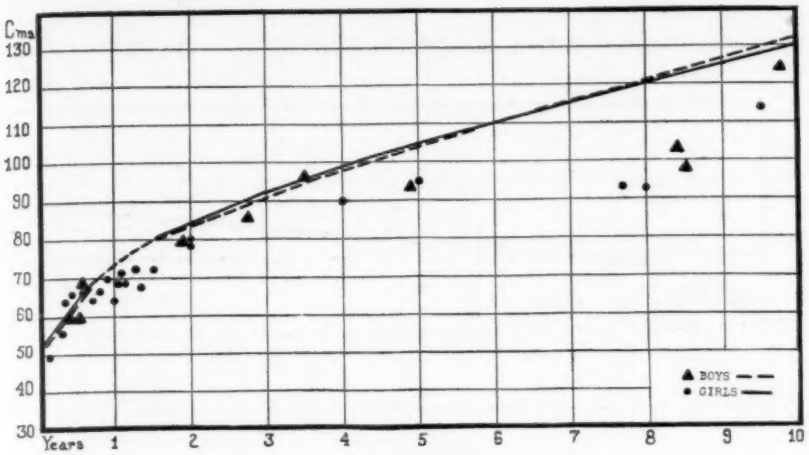

Chart 1.—Height referred to age.

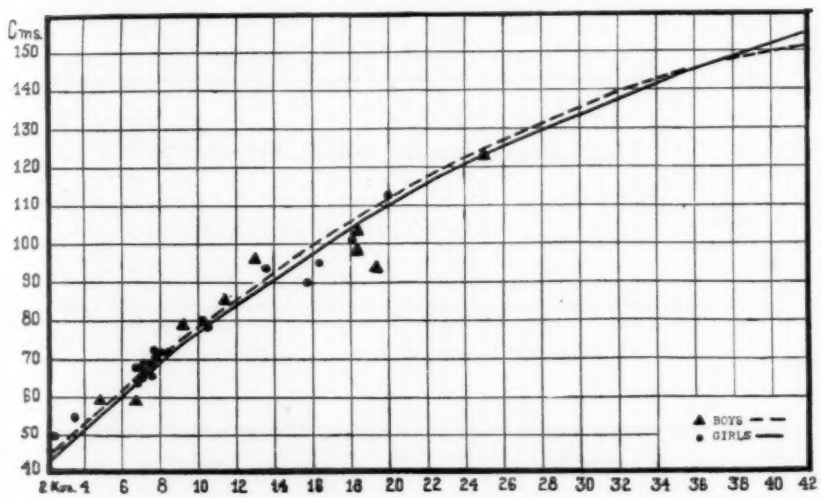

Chart 2.—Height referred to weight.

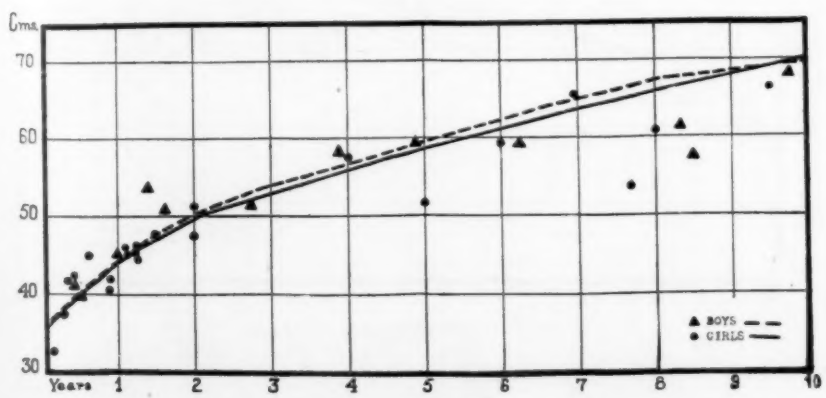

Chart 3.—Sitting height.

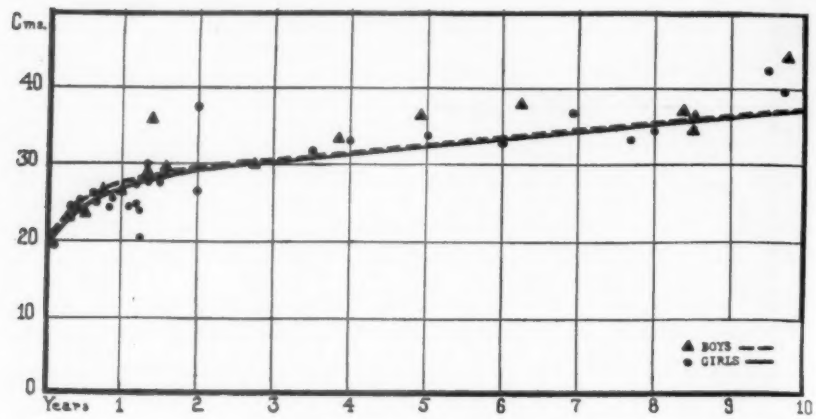

Chart 4.—Length of trunk

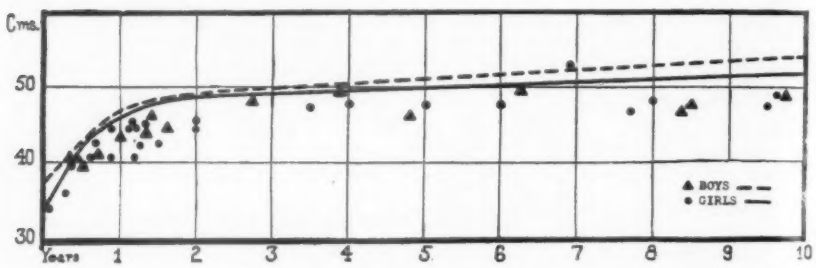

Chart 5.—Circumference of head.

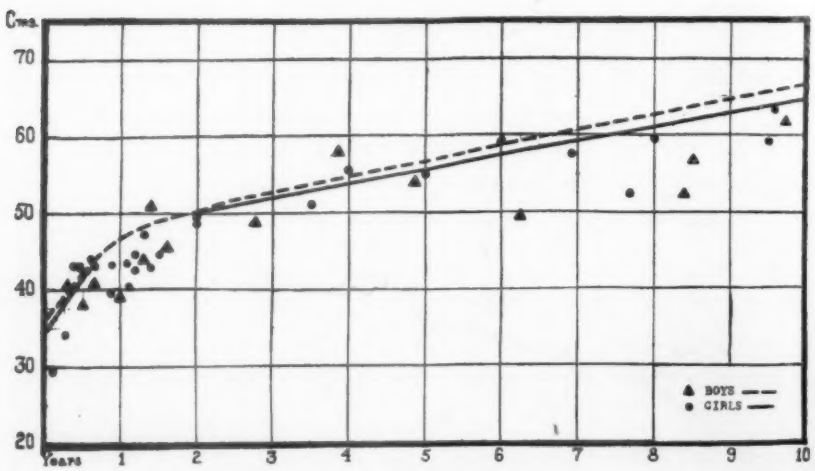

Chart 6.—Circumference of chest.

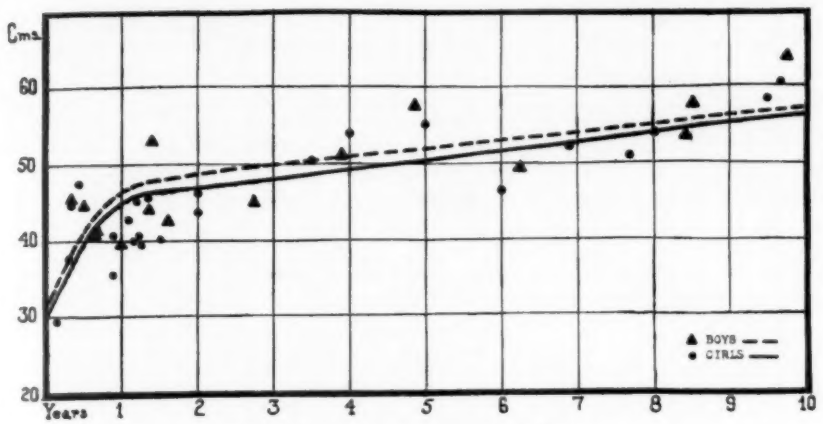

Chart 7.—Circumference of abdomen.

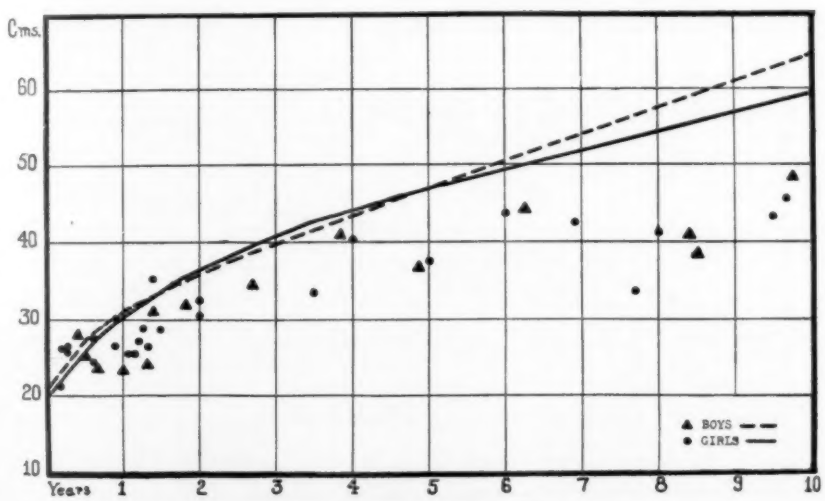

Chart 8.—Length of arms.

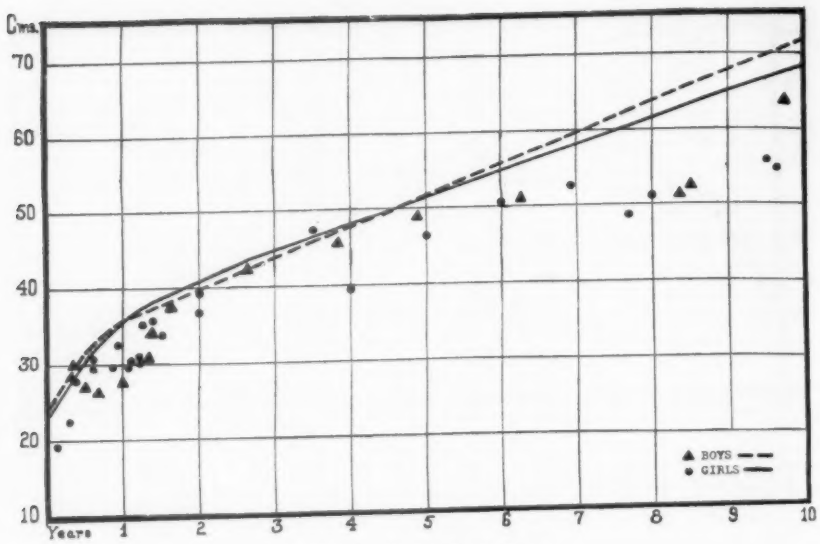

Chart 9.—Length of legs.

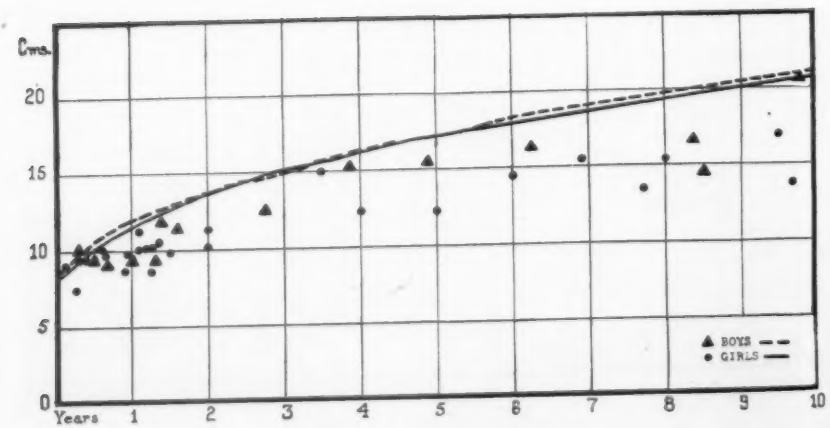

Chart 10.—Length of foot.

The characteristic flattening of the posterior skull, with the consequent shortening of the anterior-posterior diameter, may be responsible for the slightly diminished circumference.

The circumference of the chest in the majority of instances was below normal and similar to that found in cretinism. This may be characteristic of the condition or explained by the prevalence of rickets in many instances. The smallness of the chest, no doubt, emphasized the apparent length of the trunk.

Measurements of the circumference of the abdomen showed a greater divergence from normal abdomens. It was observed clinically in many cases that the abdomen protrudes beyond the level of the chest when the child is recumbent.

The greatest deviation was found in the measurements of the extremities. The length of the arms, like those of the cretin, were shorter than the average; the deviation from the normal being about the same in the two conditions, up to about 2 years of age, after which time the arms of untreated cretins tend to be shorter than those of untreated mongols.

Similar findings were observed in the legs. The tendency for the legs to be shorter than the normal was less pronounced in mongols than in cretins.

Measurements of the length of the foot were shorter than the normal foot, especially after the first year of life.

SUMMARY

There are several factors of growth in common between the cretin and the mongolian idiot. The arms, legs and feet of both conditions tend to be shorter than the normal, more so in the former than in the latter. The greatest difference in their physical measurements is noted in the circumference of the head; that of the mongolian idiot is less than normal while that of the cretin falls within normal limits.

These charts show the expected physical development of untreated mongolian idiots, and may be used for comparison in measuring the effect of treatment on the physical development. If after treatment the growth of various parts of the body follows the trend of growth of the untreated mongol, treatment is without effect, but if the growth approximates or reaches the normal curve, treatment may be said to have influenced growth.

THE PROGNOSIS OF SEQUELAE OF EPIDEMIC ENCEPHALITIS IN CHILDREN *

ROGER L. J. KENNEDY, M.D.
Fellow in Pediatrics, the Mayo Foundation
ROCHESTER, MINN.

In a consideration of the sequelae of epidemic encephalitis, the course of which is so difficult to affect by treatment, the question of prognosis is of the utmost importance. In the absence of data on former epidemics, a close observance of the progress of a series of cases offers the greatest amount of information for determining the probable outlook in any individual case.

Symonds [1] writes, in 1921, that in the subacute stage of the disease a prognosis as to the probable duration and recovery must be uncertain for several months. He found no statistics available regarding the percentage of cases in which complete recovery takes place.

Since 1921 there have been many reports of the sequelae of encephalitis, and several articles deal with these features of the disease as observed in children. Paterson and Spence [2] are in agreement with others in reporting the frequency of occurrence of sequelae. In twenty-five cases studied by them, sequelae were found in 75 per cent. They assert that mental changes vary from very mild to complete idiocy, and that they may manifest themselves as character and habit affections. The younger the child at the onset of the disease, the greater the degree of mental deficiency that follows. Strauch summarizes Hofstadt's [3] views on prognosis: "Agrypnia seems to be capable of improvement eventually, while the amyostatic complexes probably are irreparable and in the course of years lead to dementia and death."

Anderson,[4] in a study of thirty-three children recovering from the acute condition, found that agrypnia was common, persistent and usually resulted in physical or mental impairment. Those with psychic behavior and habit changes did not improve. Ebaugh [5] studied seventeen children in regard to the neuropsychiatric sequelae, and as 50 per cent.

---

* Received for publication, May 21, 1924.

1. Symonds, C. P.: Encephalitis Lethargica, Quart. J. Med. **14**:283-308 (April) 1921.

2. Paterson, D., and Spence, J. C.: The After-Effects of Epidemic Encephalitis in Children, Lancet **2**:491-493 (Sept. 3) 1921.

3. Hofstadt, F.: Encephalitis in Children, Ztschr. f. Kinderh. **29**:190 (June) 1921.

4. Anderson, Grace H.: Sequelae of Epidemic Encephalitis in Childhood, Quart. J. Med. **16**:173-192 (April) 1923.

5. Ebaugh, F. G.: Neuropsychiatric Sequelae of Acute Epidemic Encephalitis in Children, Am. J. Dis. Child. **25**:89-97 (Feb.) 1923.

of them were well or improving, he felt that the prognosis should be guarded, but that the outlook was not necessarily bad. Sherman and Beverly,[6] who subjected twenty children with deterioration difficulties to psychometric tests, report about the same percentage of cases improved in behavior.

From 1918 to 1924, fifty-nine children were admitted to the Clinic because of sequelae of epidemic encephalitis. After a complete examination, some were sent to local hospitals for further study and treatment, and others were returned to their home physicians. Subsequent visits and correspondence with parents and physicians have made it possible to keep in close touch with fifty-one of these patients. An effort has been made to determine the general course of the condition of each patient, and to trace the progress of the various syndromes and their effects.

As very few children suffer from a single sequela, it is difficult to draw conclusions as to which sequela may be responsible for certain manifestations. In Table 1 all the cases followed are analyzed briefly, and in Tables 2, 3, 4 and 5 the four prominent syndromes are reported more in detail. From the tables it is possible to get an idea of the condition of these patients on entrance to the Clinic, and of their present condition. In addition, the individual syndromes are grouped so that the changes that have occurred are evident.

There were twenty-nine boys and twenty-two girls (Table 1). The ages at the onset of the trouble ranged from 1⅓ to 12 years. The duration of the sequelae varied from 1 to 5 years. As estimated by the parents, the children were regarded as having become worse in seven instances, better in eighteen and apparently stationary in twenty-seven. One child died from an intercurrent infection. It may be noted in the tabulations that the term "better" is more or less relative, as many of the children, whose parents regard them as better, are very greatly impaired both physically and mentally, and their condition is such that substantial improvement could not be expected. Of six children, aged 3 years or under, five are now practically helpless, which bears out the observations that the sequelae are more severe in the very young.

THE RESPIRATORY SYNDROME

Although the after effects of encephalitis are all unusual, perhaps the most bizarre is the so-called respiratory syndrome. During, or some time after, the acute illness the patient begins to breathe abnormally. Usually the respirations consist of a spell of hyperpnea lasting for a

6. Sherman, M., and Beverly, B. I.: Deterioration in Children Showing Behavior Difficulties After Epidemic Encephalitis, Arch. Neurol. & Psychiat. **10**:329-343 (Sept.) 1923.

few seconds or a minute, followed by a period of apnea, or perhaps more properly breath-holding. The hyperpnea may be quiet, but usually is very noisy and of a puffing character, so that the respirations are audible at a great distance. In several instances the abnormal respiration has been interpreted by the parents as a cough, and the patient has been brought in because of this.

Most of the children displayed various forms of hyperactivity during the spells. This hyperactivity varied from slight twitching of the fingers to marked changes in posture and action, such as hyperextension of the head and neck, leaning forward in bed with the head between the knees, jumping out of bed and running around and performing all kinds of strange acts. A few patients had less noticeable respiratory disturbances, such as constant hiccough and blowing of the nose. The disturbances do not occur during the hours of sleep.

Twenty children presented the respiratory syndrome. Parker [7] has reported three of these cases. Seventeen of the twenty have been traced up to the present time. With one exception, all had moderate or severe forms of the sequelae. Although at first these cases were considered by most writers as hysterical, later study has disclosed evidence that they are undoubtedly after effects of encephalitis. In this connection it is interesting to note that although the parkinsonian, sleep, behavior, and personality syndromes are usually recognized as sequelae of encephalitis, the respiratory syndrome, in a great number of cases, is not attributed to this disease. None of the twenty cases seen at the Clinic had been ascribed to encephalitis prior to their admission. In addition to these cases, several inquiries have been received from physicians, who describe the syndrome quite fully, and ask for a probable diagnosis. As this syndrome must be fairly common, judging from the incidence of about 30 per cent. of this series, it seems advisable to report here several cases illustrating the variations of the syndrome.

REPORT OF CASES

Case 1.—S. L., a boy, aged 8 years, was admitted to the clinic, Sept. 15, 1922, because of nervousness and a change in his habits. The father was in a sanatorium because of pulmonary tuberculosis. The boy's past history was negative. In the spring of 1920 he became restless; he was sleepless and noisy at night and drowsy during the day. His behavior after a year was markedly changed, so that by the spring of 1921 he was a different boy. He had to be kept awake during the day so that he might sleep at night. He developed a constantly changing repertoire of habits. At times he was noisy; he wore a girl's dress over his clothes; on one occasion he went about with a knife, threatening to stab and kill someone; again, he was jumping and singing; for two and one-half months he walked on his hands and knees; he resorted to wriggling as a means of locomotion for three months; for five months he went about naked when he could manage to do so; at times he bit his finger and

7. Parker, H. L.: Disturbances of Respiratory Rhythm in Children, Arch. Neurol. & Psychiat. **8**:630-638 (Dec.) 1922.

toe nails. He was noisy, restless, disobedent and impulsive, and had a marked desire to display his powers. For two years he had been spitting constantly and having spells of noisy, irregular breathing. His respiratory disturbance was more common on arising and retiring and before meals. He would sit up in bed to perform, bending far over with his head between his knees and puffing loudly. Then, sitting upright, he would hold his breath or, leaning forward with his head between his knees, puff loudly.

At examination the child appeared somewhat undernourished, was restless, impulsive, explosive, emotional and curious. He had intermittent attacks of loud breathing with expiration through his nose. Between these, his breathing was imperceptible, with occasional breath-holding spells lasting from twenty to thirty seconds, when, with mouth open and staring straight ahead, he became slowly cyanosed, but answered immediately when spoken to. Spitting, drinking water, and asking to go to the toilet to urinate occupied the greater part of his attention. All the reflexes were hyperactive; there was a bilateral positive Babinski sign.

The patient has improved somewhat since his first examination; he sleeps better; his behavior has improved; he now has the habit of chewing his tongue; he continues to spit and his breathing spells are unchanged. His mental tests show no change since the onset of the trouble; his mental age is 6 years and 4 months.

CASE 2.—M. S., a girl, aged 14 years, was admitted to the clinic May 25, 1922, because of headache. Although the other members of the family had had influenza, she had not been affected by it and was in good health until February, 1920. At this time she became restless, rolled and tossed about in bed and complained of cramps in the arms. After a week the restlessness decreased, but the nervousness and cramps persisted. Four months later, she began to have a dry cough, which shortly became continuous, so that it interfered with eating and talking. Almost every expiration was replaced by a cough. A little later she began to have spells of breath-holding. Then attacks developed during which she would jump out of bed, cross her arms with her hands on her shoulders, bend forward and breathe forcibly and whimper as if in distress, then straighten up and hold her breath for a while. After repeating this procedure several times she would get back into bed and lie more quietly than at any other time. Several months later she developed grand mal attacks.

At examination in the hospital she appeared moderately undernourished. The skin was pale. The left pupil was slightly larger than the right. The knee and ankle jerks were very active. While lying quietly in bed she behaved and talked intelligently. She would begin to breathe more deeply and to cough, taking a deep inspiration and replacing the expiration by a cough. The face assumed a distressed expression. After about five minutes of such breathing, she would jump out of bed, stand erect or walk about the room, cross her arms with her hands on her shoulders, bend forward and breathe very forcibly for several inspirations, then straighten up and hold her breath for a half minute or so and then repeat the bending and hard breathing. When she talked during such spells, she had a whining complaining voice. During the spells she was contrary, imperious, and demanded that the nurse fix her bed or move the furniture around. After several repetitions of bending and breath-holding she would suddenly run to bed and lie quietly. After remaining quiet for some time, she gradually became more active and then repeated the whole performance.

After a period of two years her respirations are still practically unchanged, although she has been free from convulsions.

CASE 3.—C. B., a boy, aged 13 years, was admitted to the clinic Dec. 20, 1923, because of nervousness. He had had measles, pertussis and mumps in early childhood, and influenza at the age of 8 years. In December, 1922, he had become nervous, cross and fretful. He took no interest in his school work

TABLE 1.—*Summary of Cases*

Case	Age at Onset, Years	Sex*	Appearance of Sequela	Duration of Sequela, Years	Character of Sequela	Condition	Remarks
1	14	♂	1919	5	Ataxic, slow movements, nystagmus	Worse	Irritable, changed disposition, inability to walk or dress, but feeds self, mentally retarded (?)
2	12	♀	1919	5	Parkinsonian syndrome, blurred vision, salivation	Same	Mentally retarded, refractory, atrophy, right arm and leg, tremor, protruding tongue
3	2	♀	1919	5	Inability to walk, talk or play; screaming, chewing fingers	Same	Mentally deficient, nervous, cries great deal, requires constant care
4	1⅓	♂	1918	5½	Blindness of right eye, deaf and dumb, mutism	Same	Deaf and dumb, blind in right eye, cares for self
5	11	♀	1923	1	Inversion of sleep, changed personality	Same	Sleep improved, sleeps from midnight to noon, excessive, incoherent, rapid praying; school, eighth grade
6	8	♂	1919	5	Changed personality, behavior changes	Same	Easily angered, steals, incendiarism, frequent headache and nose-bleed, school for feebleminded for one year, State Reformatory since Oct. 7, 1923
7	12	♂	1920	3½	Parkinsonian syndrome	Same	Irritable, difficulty in walking, falls frequently, impaired speech
8	7	♀	1920	4	Changed personality, spasticity of right leg, strabismus	Same	Irritable, quick tempered, bites finger nails, walks with difficulty, school, fourth grade
9	2	♀	1918	5	Right hemiplegia, convulsions, does not talk or recognize parents	Worse	Cannot talk, sleepless, right hemiplegia, childish, one convulsion in three years
10	3	♂	1920	4	Unable to walk, purposeless acts	Better	Dumb, helpless, vomits everything except evening meal; has lived on one meal a day for eighteen months
11	4½	♂	1919	5	Respiratory syndrome, petit mal, insomnia and nocturnal hyperkinesis	Same	Restless in sleep, respirations unchanged, petit mal, cares for self and is up and about
12	13	♀	1922	2	Respiratory syndrome, fear of choking, feeling of dyspnea, insomnia	Better	Respiratory disturbance when on back or in bed
13	9	♂	1919	5	Parkinsonian syndrome, irritable	Worse	Mental retardation, irritable, speech and walking impaired greatly, falls frequently, unable to care for self
14	10	♀	1920	4	Chorea, insomnia and nocturnal hyperkinesis, respiratory syndrome with postural change, personality changed	Better	Mental retardation, respiration normal except when excited, speech slow, sleeps long time; slow movements, cares for self
15	8	♂	1921	2½	Parkinsonian syndrome, insomnia and nocturnal hyperkinesis, changed personality	Same	Changed personality, weak, tremor marked, requires help except for eating, attends district school, no progress
16	11	♂	1920	4	Inversion of sleep and nocturnal hyperkinesis, changed personality	Better	Sleep nearly normal, tires easily, cares for self, school, eighth grade
17	9	♂	1920	4	Parkinsonian syndrome, adiposity	Same	Irritable, impaired walking, falls frequently, stutters, restless, requires help, school, fifth grade
18	10	♂	1920	4	Parkinsonian syndrome, complete change of personality, voracious appetite, sialorrhea	Worse	Irritable, left side partly paralyzed, contraction of left leg, great difficulty in walking, tremor, sleep disturbance, feeds self, requires help
19	2½	♂	1922	2	Convulsions	Better	No convulsions for nine months
20	9	♂	1919	4½	Parkinsonian syndrome, respiratory syndrome	Worse	Almost helpless, speaks very little, respirations heavy and noisy
21	1⅓	♀	1919	5	Respiratory syndrome, with kicking, twisting and writhing, mental deficiency	Worse	Respiration improved, mental deficiency, helpless
22	8	♀	1920	4	Changed personality, marked behavior changes	Better	Mental retardation, very emotional, drowsy at times, school for feebleminded
23	12	♀	1920	4	Respiratory syndrome, changed personality, convulsions	Worse	Mental retardation, no more convulsions, somewhat more nervous, partly cares for self

24	6	♂	1920	3½	Inversion of sleep with nocturnal hyperkinesis, respiratory syndrome, changed personality and behavior	Better	Respirations heavy at times, sleep disturbance improved, quarrelsome, polydypsia, urinary incontinence, talks continually
25	5	♀	1918	5½	Changed personality, marked behavior changes, insomnia, mental retardation	Same	Mental retardation, apparently unconscious of surroundings, talks and spells when told to do so, school for defective children, kindergarten
26	7	♂	1919	4½	Inversion of sleep, respiratory syndrome, changed personality	Better	Occasional hyperpnea, abnormally loving disposition, too restless for school, acts like baby
27	11	♂	1919	5	Parkinsonian syndrome, behavior changed	.....	Died Jan. 3, 1923, of intercurrent infection
28	10	♂	1919	4½	Parkinsonian syndrome, inversion of sleep	Better	Sleep practically normal, very wilful and mischievous, school, seventh grade
29	11	♂	1920	4	Parkinsonian syndrome	Same	Weaker, unable to walk or talk well, unable to dress or feed self
30	9	♂	1922	2	Respiratory syndrome, vertigo and falling	Better	Respiration improved but still abnormal, cares for self
31	6	♂	1922	2	Inversion of sleep, nocturnal hyperkinesis, behavior changes, sialorrhea	Better	Irritable, respiratory difficulty, speech impaired, sleep disturbance continues, school, second grade
32	6	♀	1920	4	Inversion of sleep, parkinsonian syndrome	Better	Walking and speech markedly impaired, cannot help self
33	8	♀	1921	3	Parkinsonian syndrome, respiratory syndrome, changed personality	Same	No effort to walk, speech poor, irritable, nervous, refuses to study. Respiration normal
34	8	♀	1923	1	Inversion of sleep, paresthesia.....	Better	Talks rapidly, sleep improved, sleeps five hours daily, movements are slow, school, seventh grade
35	8	♂	1922	2	Parkinsonian syndrome	Same	Unable to walk, speech difficult, cannot care for self
36	9	♀	1923	1	Changed personality	Better	Quick tempered, behavior changed, night terrors, State Graded School, fifth grade
37	9½	♀	1923	1	Inversion of sleep, nocturnal hyperkinesis, respiratory syndrome	Same	Sleeps somewhat better, less nocturnal activity, respiratory disturbance still very marked
38	11	♀	1921	3	Parkinsonian syndrome	Same	Walking more difficult, speech poor, tremor marked, unable to care for self
39	7	♀	1923	1	Inversion of sleep, changed personality, sialorrhea	Better	Irritable, walks excessively, marked expectoration, speech not clear, cares for self, school, third grade
40	11	♂	1921	3	Respiratory syndrome, changed personality	Same	Irritable, unmanageable, respiration unchanged, cares for self, school, seventh grade
41	4	♂	1923	1	Changed personality, grand mal, mental deterioration	Same	Mental deterioration, walks very little, fewer convulsions, nervous, frequent vertigo
42	2	♂	1922	1½	Changed personality, constant swallowing	Better	Cross and irritable, respiration rapid at times
43	13	♀	1923	1	Inversion of sleep and nocturnal hyperkinesis, respiratory syndrome	Same	Unchanged
44	8	♀	1921	3	Parkinsonian syndrome, changed personality	Same	Bilateral seventh nerve palsy, otherwise unchanged
45	7	♂	1919	4	Inversion of sleep and nocturnal hyperkinesis, changed personality, parkinsonian syndrome, sialorrhea, polydypsia	Same	Sleep disturbance lasted two years, parkinsonian syndrome typical
46	9	♀	1919	5	Inversion of sleep, nocturnal hyperkinesis, parkinsonian syndrome	Same	Sleep normal after one year, parkinsonian syndrome more marked
47	12	♂	1923	1	Inversion of sleep and nocturnal hyperkinesis, respiratory syndrome	Better	Sleep improving, respiration unchanged, much better in other respects, school, eighth grade
48	11	♂	1920	4	Respiratory syndrome	Same	Feebleminded, breathing abnormal and accompanied by change in posture, in institution for feebleminded
49	12	♂	1923	1	Inversion of sleep and nocturnal hyperkinesis, respiratory syndrome	Better	Sleeps normally, apnea and hyperpnea somewhat less marked
50	7	♀	1922	2	Respiratory syndrome with marked postural changes	Same	Breath-holding, hyperpnea, falling
51	7	♂	1919	5	Inversion of sleep, parkinsonian syndrome, obesity	Same	Partial paralysis of left side, weakness, slow speech, gained 25 pounds (11 kg.) in two years

* In this column, ♀ indicates female; ♂, male.

when in school, but worried about it when at home. Jan. 7, 1923, he complained of pain in his left elbow which came at night and was always sharp. Five days later, the pain was felt in the right elbow and then gradually subsided. January 13, his arms, hands and trunk began to "shake." There were continuous, short, jerky contractions of the muscles of the chest, abdomen, neck, arm and hand muscles. These were accompanied by rapid, jerky respiratory movements. In spite of the jerking, he had fair control of his arms and hands. At this time his temperature rose and remained at from 100 to 101 for ten weeks. On the fourth day of the trouble he had diplopia and became unconscious and delirious. He remained so for ten days, after which he gradually became rational, although the jerking continued. He developed a marked disturbance of sleep so that he retired at midnight and rose at noon. Before going to sleep at night he would blow his nose constantly for long periods. When he was more tired than usual he was unable to sleep well and was restless and irritable.

At examination the boy appeared rather thin, but was almost normal in weight. The left pupil was somewhat larger than the right, and slightly eccentric. Respiration seemed to consist of a regular series of spasms of the respiratory muscles which simulated hiccough, and which were accompanied by synchronous single contractions of the fingers, especially of the left thumb, index and small fingers. He carried his head bent forward and inclined slightly to the right, although he could control its position when told to do so. His voice had a nasal quality. The knee jerks were moderately increased; the Chvostek sign was marked. He appeared to be bright, intelligent and well behaved.

At present he is somewhat improved. He attends school for three hours each day; he is in the eighth grade; his behavior and disposition are much better and he sleeps considerably better. His respirations and the jerking which accompanies them are about the same as they were fourteen months ago.

Case 4.—J. M., a boy, aged 13 years, entered the clinic July 12, 1923, because of mental trouble. His past history was negative except for measles, mumps, pertussis and influenza. In February, 1921, he had had an attack of epidemic encephalitis and was lethargic for a week. He returned to school after three weeks, although he was still quite drowsy. From the time of the onset of his illness he underwent a gradual change in disposition. He became less able to apply himself in school, and in May, 1923, was removed because of inattentiveness, the habit of throwing objects around the room and annoying other pupils. At the same time he begun to show an exaggerated affection for his mother, brothers and sisters. For the last two years he had been breathing abnormally. For periods of hours he would breathe rapidly and noisily through his mouth.

Examination showed a boy of normal height and weight. He was apparently very drowsy and went to sleep several times during the examination. He had slight left divergent strabismus and slight ptosis of the left upper eyelid. His face was expressionless. He breathed through his mouth, rather noisily and at the rate of fifty respirations a minute. The knee jerks and ankle jerks were moderately increased.

Although his drowsiness and misbehavior have now practically disappeared, and although he appears to be quite himself when he is not breathing heavily, as soon as the noisy hyperpneic respirations begin he seems to lose control of himself. He becomes cross and unmanageable and extremely trying to his parents.

Case 5.—M. R., a girl, aged 10 years, entered the clinic April 16, 1923, because of restlessness, "stiff" gait, slouchy position when sitting or standing, and tremor. She was well until February, 1919, when she had influenza. In February, 1921, she had acute epidemic encephalitis, followed by inversion of the sleep rhythm and nocturnal hyperkinesis. Gradually she developed a parkinsonian syndrome and a change in disposition. She frequently took deep, sighing respirations, which she had never done previous to her illness.

Examination showed a girl considerably under normal weight. There was nystagmus in all directions. She presented the typical picture of a parkinsonian syndrome.

Though the parkinsonian syndrome has persisted the respiratory trouble has disappeared and has not troubled her for a year.

COMMENT

The condition does not appear to be so hopeless as some of the other sequelae, as there is no apparent deteriorating effect. During the spells of irregular breathing the patients act quite abnormally, but when

TABLE 2.—*Respiratory Syndrome*

	Original Syndrome		Present Condition	
Case	Respiration	Synchronous Movements	Respiration	Synchronous Movements
48	Breath-holding hyperpnea	Marked postural changes, falling	Breath-holding hyperpnea	Marked postural changes, falling
12	Deep, regular	Fear of suffocation, dyspnea	Hyperpnea, in bed, when on back, or sitting quietly	
20	Deep, noisy		Deep, noisy	
21	Apnea, hyperpnea noisy, puffing	Kicking, twisting, writhing	Apnea, hyperpnea	Kicking, twisting, writhing
23	Apnea, hyperpnea	Marked hyperkinesis	Apnea, hyperpnea	Marked hyperkinesis
24	Apnea, hyperpnea	Marked postural change	Apnea, hyperpnea	Marked postural change
26	Apnea, hyperpnea	.....	Occasional apnea and hyperpnea	
30	Hyperpnea, hard, irregular breathing	.....	Improved, hyperpnea	
33	Deep, sighing	.....	Normal	
37	Apnea, hyperpnea, loud, puffing	Holds nose and expires forcibly through it	Apnea, hyperpnea, loud, puffing	Holds nose and expires forcibly through it
39	Blows nose constantly	.....	Normal	
40	Rapid, noisy	Becomes cross, unmanageable	Rapid, noisy	Becomes cross, unmanageable
43	Loud, puffing	.....	Loud, puffing	
47	Rapid, jerky inspiration, resembling hiccough	Jerking of diaphragm and fingers	Jerky respiration	Jerking of fingers
49	Apnea, hyperpnea	Slow purposeless movements of arms and hands	Apnea, hyperpnea	Slow purposeless movements of arms and hands
50	Breath-holding, hyperpnea	Falling, holding head backward	Breath-holding, hyperpnea	Falling, holding head backward
14	Apnea, hyperpnea	Marked postural change and hyperactivity	Abnormal only under excitement	Slight hyperactivity

the spells cease they appear like other children, provided, of course, that they have no other sequelae. A girl, aged 13 years, was examined at the clinic, having been sent in alone and without letters. She complained of a cough which had persisted for several months following an attack of influenza. The preliminary examination was negative, and she was placed in a boarding house, to return the next day for further study. At twelve o'clock that night she had to be removed to the hospital because "she was puffing like a steam engine" and keeping the other inhabitants of the house awake.

The severity of the respiratory syndrome is apparently limited, and does not progress beyond a certain degree. Having reached this, it tends to remain stationary or to improve. One patient, with a constant habit of blowing the nose and another with deep sighing inspiration, now exhibit no respiratory disturbance. Three are considerably improved, and the others are slightly improved or their condition is stationary. In none has the condition become worse (Table 2).

PARKINSONIAN SYNDROME

There were twenty-one cases of juvenile paralysis agitans or parkinsonian syndrome, the history and clinical picture of which is well brought out by the following abstract of a case record.

CASE 6.—A. G., a girl, aged 13 years, entered the clinic Dec. 27, 1923, with the complaint of partial paralysis of the left side. She had been well until March, 1919, when she had a mild attack of influenza. Two weeks later she developed acute epidemic encephalitis of the choreic type, the febrile stage lasting one week. The choreiform movements persisted in severe form for a year, during which she slept only two or three hours in two or three days, her sleep always coming in the day time. Gradually during the next year her sleep improved and for the two years before examination had been normal. During the last four years she had gradually developed a mask-like expression, marked drooling of saliva, tremor of the hands and arms, and spasticity of the arms and legs, more marked on the left side and general weakness.

Examination showed a girl of normal height and weight. The left pupil was slightly larger than the right and there was slight horizontal nystagmus. The face was mask-like. There was tremor of the tongue when protruded, and also of the arms and hands, especially on the left side. She sat and stood with a forward inclination of the body. The gait was spastic, the left leg being more spastic than the right. There was a tendency to fall to the left. Propulsion and retropulsion were present. The speech was slurring so that most of her remarks were unintelligible. Although response to questions was slow, her answers were intelligent and she appeared mentally alert, but not bright. Laboratory examinations were negative.

At present she eats and sleeps well and has no bladder or bowel disturbance.

COMMENT

The ages of the twenty-one patients with the parkinsonian syndrome ranged from 7 to 14 years at the time of onset. When some of the children entered the Clinic the picture of a parkinsonian syndrome was not complete, but there were enough cardinal features to warrant the diagnosis. Subsequently all of them developed the syndrome in its entirety. One child died from an intercurrent infection four years after the onset of encephalitis. Not a few patients who are suffering from sequelae show perhaps one or even several signs that belong to this syndrome when they are first seen. In cases of this type the diagnosis must be tentative, for, with the manifold forms which the sequelae may assume, there is, obviously, chance for error.

The outlook in this condition is bad. Beginning more or less insidiously with tremor, awkwardness, mask-like expression, or one of the other features of the disease, it progresses until fully developed. Having reached this stage it appears to come more or less to a standstill. The general weakness apparently increases, but as most of these children make little effort to exercise, the weakness may well be due, at least in part, to voluntary inactivity. At present, of the sixteen children traced, only two are able to take part in school work and they must be transported to and from school.

In spite of the marked physical impairment and slow reaction time, it has been noted here and elsewhere, that there is very little effect on the mentality. These children learn and remember, but the time and effort required to elicit an answer from them leads to the idea that they are mentally deficient.

TABLE 3.—*Condition at Present of Patients with Parkinsonian Syndrome*

Case	Attitude	Gait	Falling	Tremor	Facies	Drooling	Speech	Strength	Mentality	School
2	Typical	Fair	.....	+	Mask	+	Slurred	Weak	Normal	
7	Typical	Poor	Frequent	+	Mask	+	Slurred	Weak	Normal	
13*	.....	Poor	Frequent	+	Mask	+	Slurred	Weak	Retarded	
15	Typical	Unsteady	.....	+	Mask	..	Slurred	Weak	Normal	Third grade no progress
17	Typical	Unsteady	Frequent	+	Mask	+	Stutter	Weak	Normal	Fifth grade
18	Cannot stand	.....	.....	+	Mask	+	Very bad	Weak	Normal	
27†	.....	.....	.....	..	.....	..	.....	.....	.....	
28	Good	Fair	.....	Slight	Mask	..	Good	Strong	Normal	Seventh grade
29	Typical	Unsteady	Frequent	+	Mask	+	Slurred	Weak	Normal	
33	Cannot stand	.....	.....	+	Mask	+	Very bad	Weak	Normal	Private tutor
35	Cannot stand	.....	.....	+	Mask	+	Slurred	Weak	Normal	
38	Typical	Paralysis	.....	+	Mask	+	Slurred	Weak	Normal	
44	Typical	Spastic	Frequent	+	Mask	+	Slurred	Weak	Normal	
45	Unsteady	Spastic	Occasional	+	Mask	+	Slurred	Weak	Normal	
46	Typical	Unsteady	Occasional	+	Mask	+	Slurred	Weak	Normal	
51	Typical	Paralysis	.....	+	Mask	..	Slurred	Weak	Normal	Seventh grade

* Paralysis. † Died Jan. 30, 1923, from intercurrent infection.

With their physical condition already such that they can do very little toward helping themselves it may be said that there is little or no hope for their recovery to anything approaching a normal condition, although the immediate danger to life is not great. The lesion, so far as known, furnishes a basis for this view. There are two main ideas prevalent as to the more exact nature and location of the lesion: one, that it is in the globus pallidus, the other, that it involves the substantia nigra. It is, nevertheless, generally accepted that there are destructive lesions of some sort in the basal ganglions. With the lack

of repair characteristic of brain tissue, it is evident that recovery in a condition resulting from the destruction thereof is not to be expected (Table 3).

DISTURBANCE OF SLEEP AND NOCTURNAL HYPERKINESIS

One of the most common and most troublesome sequelae of encephalitis in children is the disturbance of sleep and the heightened psychomotor activity which accompanies it. The hours of sleep are often completely reversed. The patient may be fairly quiet during the afternoon, but toward evening displays increasing signs of restlessness and hyperactivity. By the time the regular hour for sleep has arrived the patient is so busily engaged in any and every conceivable form of activity that he is in almost constant motion. Talking, singing, whistling, yelling, running, jumping, rolling, pulling and pushing, or rearranging bed clothes and furniture are only a few of the things which may occupy him. Until eleven or twelve o'clock at night or even five or six in the morning, this activity continues, the patient showing absolutely no inclination to sleep. Toward morning he becomes more quiet, and finally falls into a sound slumber from which he cannot be aroused until perhaps the following noon or afternoon. Many forms of treatment have been tried for this disorder, including hypnotics and sedatives. None has proved effective in more than a very few cases. The following case is an example of this disturbance, and, in addition, shows a combination of sequelae, and illustrates how sequelae may develop and subside to be followed by others

CASE 7.—F. B., a boy, aged 11 years, entered the clinic Nov. 12, 1923, on account of weakness. In December, 1919, he had had a mild attack of encephalitis. About four days later, his habits of sleep were noticeably changed. For two years he did not sleep at night, but remained awake, very active, pulling the bed to pieces, noisy, yelling, talking and running about the room. Toward morning he became quiet and slept during the day in two or three hour periods, waking and crying between times.

The third year of the trouble he began to sleep at night, but his behavior was entirely different from what it had been before his illness. He became irritable, cranky and quarrelsome at home. He would go out of doors and run until exhausted; then he would fall or return home and sleep a short while, repeating these actions as soon as he awoke.

During the last year, the fourth since the onset of his illness, he has gradually developed an expressionless face, drooling, spastic gait, unstable station, tremor of the arms and body and very slow movements and speech. He takes an hour or two to eat his meals, and even longer to dress. He is still irritable, unreasonable in his demands, quarrelsome with his sister and goes into fits of anger if he is refused anything. He talks a great deal during the day when he is exercising, but when he stops his physical exertion he is sleepy and drowsy. He has developed an excessive thirst and the habit of constant spitting (sialorrhea).

Examination showed a boy of normal height and weight. His face was expressionless, except for frequent silly grins. He drooled considerable amounts of saliva; his station was unsteady; his gait was spastic and somewhat ataxic, and he staggered as though intoxicated. Rigidity of the arms, of "lead-pipe"

character, was present. The knee jerks were markedly increased. Answers were made slowly but very intelligently. He could spell the name of his home town very slowly.

COMMENT

So far as the sleep disturbance is concerned, the picture presented by nineteen children of this series was very similar to that of the foregoing case. The inversion of the time of sleep, a decrease, in some cases, of the total sleeping time, and the nocturnal hyperactivity are the chief features. Only three of the nineteen have failed to improve in their habits of sleep since being under observation. Nine of the others are now sleeping normally, or nearly so. A parkinsonian syndrome developed in two children after the cessation of the sleep disturbance.

In the children with sleep disturbance and without other syndromes, such as Parkinson's, improvement has been of a general nature, so that

TABLE 4.—*Condition of Patients with Sleep Disturbance*

	Original Syndrome		
Case	Inversion of Sleep	Nocturnal Hyperkinesis	Present Syndrome: Sleep
5	+	..	Retires at midnight, rises at noon
12	+	..	Nearly normal, marked improvement
11	+	+	Improved, sleep restless
14	+	+	Normal, sleeping time increased
15	+	+	Improved, sleeps eleven hours
16	+	+	Nearly normal
24	+	+	Somewhat improved, awake all night at times
25	+	+	Normal
26	+	..	Normal
28	+	..	Nearly normal
31	+	+	Unchanged, wakes easily, sleeps on hands and knees
34	+	+	Retires from 2 to 6 a. m., sleeps five hours, wakes easily
37	+	+	Slight improvement, nocturnal hyperkinesis less marked
39	+	+	Nearly normal
43	+	+	Unchanged
45	+	+	Normal after two years, followed by parkinsonian syndrome
47	+	+	Somewhat improved, sleeps late in morning
46	+	+	Normal after one year, followed by parkinsonian syndrome
49	+	+	Retires from 11 p. m. to 4 a. m., apnea and hyperpnea while awake.

of all the groups these children seem to have the least permanent impairment. In the presence of other sequelae, the child may recover from the sleep disturbance, but still be markedly impaired mentally (Table 4).

CHANGE IN PERSONALITY AND BEHAVIOR

Very few patients who recover from an acute attack of encephalitis fail to show some effect of the illness for a long time. The effect may be of little consequence and evinced only by a slightly altered mannerism, or it may be so great as to cause an entire change in the patient, mentally and physically. This has been true very often of children, a large percentage of whom show changes of a sufficient degree to be included in the group with distinct alteration of personality and behavior.

The variety of manifestations of change seems to be almost without limit. Every conceivable act, occasional or habitual, and all of the different psychic and emotional states are displayed by these patients. The following case is an example.

Case 8.—A. F., a boy, aged 10 years, was brought to the clinic May 9, 1922, because of nervousness. In March, 1920, he had influenza followed by an acute attack of encephalitis which lasted eight days. For a month afterward he was drowsy and had diplopia. He improved gradually and returned to school, but had to be taken out because he asked so many questions and removed books from other desks to his own. At times he went to sleep in school and slept for hours.

In September, 1920, another attempt was made to have him attend school, but this was soon given up as he started to steal at random. He took a diamond ring belonging to his sister and disposed of it for an automobile ride. He began to enter stores and take things which he later gave away. When questioned in regard to his stealing, he invariably replied that he heard a voice in his left ear which forced him to do so, and when asked why he gave the stolen objects away, he replied that it was in order to be good to people.

He began to run away from home, leaving at any hour and remaining out all night, sleeping in church, on the porch or in other places. He called at the houses of strangers, telling them that his parents were dead, that the hired girl was cruel and that he was hungry. He usually succeeded in getting a meal from them. He got into the automobiles of strangers, and with his entertaining manners would be given rides for hours at a time. He would never tell anything that happened on these occasions, saying "yes" and "no" to leading questions, but these answers were often incorrect and when confronted with the real facts he could be made to admit them. In explanation of these acts he constantly maintained that there were two voices in his ears on these occasions, the one of the devil telling him to run away, and the other of an angel telling him not to do so. At times he would go for days or even a week without running away or stealing, both of which acts would come in spells. Then he would suddenly go to his father, and tell him to watch him as he was hearing the command to run away. Even after telling his father to watch, he displayed cunning in trying to get away.

He could not play with other children on account of his overbearing manner and his fits of anger. His parents had great difficulty in controlling him, though there were periods in which he appeared perfectly normal. He had been twice before the Juvenile Research Bureau of the city in which he lived; the first time it was advised that he be given a free rein and, this failing, severe discipline was advised. He had come under the notice of the court in a neighboring town.

Examination disclosed nothing attributable to the encephalitis. A prolapsed rectum was treated surgically. According to the Stanford revision of the Binet-Simon test the boy's mental age was found to be normal and the intelligence quotient was 100 per cent. In spite of the mental test, the boy required institutional care and was sent to the State School for the Feebleminded. Since being there he has improved somewhat, but his general condition is not greatly changed.

COMMENT

This case illustrates the main features to be considered in dealing with children who are suffering from this syndrome. In the first place the absolutely different personality which they display is well exemplified. They are apparently acting in response to a most urgent stimulus,

which they are powerless to resist. Second, and perhaps of most importance, is the consideration of the mental status. As has been indicated, there is no evidence to show that a considerable proportion of such patients are mentally retarded or deficient. As Anderson has suggested, they are moral rather than mental imbeciles. Some of them appear dull and drowsy, but in their antics and behavior they display

TABLE 5.—*Condition of Patients with Changed Personality and Habits*

	Original Syndrome		Present Syndrome		
Case	Behavior Change	Personality Change	Behavior	Mentality	Other Syndromes
5	Marked	Marked	Restless, prays frequently, throws kisses at night, eighth grade, third on honor roll	Normal	Sleep inversion
6	Marked	Marked	Irritable, steals, incendiarism, State Reform School	Normal	None
8	Marked	Marked	Very irritable, bites finger nails, fourth grade in public school	Normal	Spasticity of leg
9	Moderate	.....	Sensitive, easily offended, restless, requires attention for everything	Retarded	Hemiplegia, mental deficiency
13	.....	Mild	Irritable, cannot care for self	Retarded	Parkinson
14	Marked	Marked	Irritable, nervous, private tutor	Retarded	Sleep inversion, respiratory
15	Marked	Marked	Irritable, district school, no progress	Retarded	Parkinson, sleep inversion
18	Marked	Marked	Irritable, restless, hyperactive, talkative, cannot care for self	Retarded	Parkinson
21	Marked	.....	Nervous, hyperactive, cannot care for self	Deficient	Respiratory, mental deficiency
22	Marked	Marked	Emotional, very unstable, school for feebleminded	Deficient	None
23	Marked	Marked	Very refractory, refuses to eat or dress, cannot care for self	Retarded	Respiratory, convulsions
24	Marked	Marked	Irritable, chews tongue, talks constantly, removed from school, quarrelsome	Retarded	Sleep inversion, respiratory
25	Marked	Marked	Irritable, unstable, unconscious of surroundings at times, School for Defective Children	Deficient	Insomnia
26	.....	Mild	Irritable, very loving, restless, acts like baby	Retarded	Sleep disturbance
31	Marked	.....	Bad temper, marked change in disposition, school one half day, second grade	Normal	Sleep disturbance
32	Marked	.....	Bites nails, cannot care for self	Normal	Parkinson
33	Moderate	.....	Nervous, resistant at times, private tutor	Retarded	Parkinson, respiratory
36	Moderate	Moderate	Quick tempered, morbid fears, State Graded School, fifth grade	Normal	None
39	.....	Mild	Irritable, quick tempered, parochial school, third grade	Normal	Sleep inversion
40	.....	Mild	Irritable, unmanageable, parochial school, seventh grade	Retarded	Respiratory
41	Marked	Marked	Characteristics of marked mental deficiency	Deficient	Grand mal
42	Mild	Mild	Quick tempered, nervous, restless, refuses to eat	Normal	Respiratory
45	Marked	Marked	Irritable, quarrelsome, talkative	Normal	Sleep inversion, Parkinson

a cunning that is not commensurate with greatly impaired mental faculties. It is difficult to estimate how much of their trouble is due to this and how much is due to other syndromes. Of twenty-three such children of whom information has been obtained, three had no other sequelae; two of these are apparently normal mentally, but their antisocial tendencies are such that they have been sent to state reform

schools, and the third, whose record has been given, is in a school for the feebleminded.

The mentality of the other twenty children, with six exceptions, is so impaired by this or other sequelae that they have made little or no progress, and some of them are worse. The six exceptions are children who are attending school and making fair progress. One of them is third on the school honor roll (Table 5).

OTHER SEQUELAE

Besides the syndromes discussed, other manifestations were displayed by a group of six children who suffered from the acute illness before the age of four years, and in whom the sequelae were most severe. One child is well; five are mentally deficient as a result of encephalitis; one is deaf, dumb, and blind; two more are high grade idiots; one suffers from a right hemiplegia, deaf-mutism, and generalized convulsions of the grand mal type and the other is mentally deficient and has grand mal attacks. Fortunately, the disease has apparently affected the younger children in only a small number of instances, but in this series of cases the effects in all except one have been severe and the prognosis is uniformly bad.

SUMMARY

Sixty-one cases of residual epidemic encephalitis in children under 14 years of age were studied. Fifty-two of the patients were traced from the time of their first visit until the present.

Twenty-one, sixteen of whom were traced, presented the parkinsonian syndrome. None was improved; the condition of two was stationary, and of fourteen, worse. One died from an intercurrent infection. The prognosis in this condition is not bad as regards life, but poor as regards improvement or recovery.

Twenty-three had changes in behavior and personality. Six were improved, and seventeen showed no improvement, or had become worse. The lack of restraint exhibited by these children does not necessarily imply any great degree of mental impairment.

Nineteen presented disturbances of sleep. Nine of these are now sleeping practically normally, three still show more or less disturbance, and seven are the same or worse.

The respiratory syndrome occurred in this series much more commonly than is indicated by the literature. Two of seventeen children who had this sequela are well; three are apparently improving, and the condition of twelve is unchanged. In none has the condition become worse.

THE EFFECT OF PREGNANCY ON THE COURSE OF SCURVY IN GUINEA-PIGS*

HENRY J. GERSTENBERGER, M.D.,
WILLIAM M. CHAMPION, M.D.,
AND
DONALDA N. SMITH, B.S.
CLEVELAND

In January, 1921, during the course of experiments to test the antiscorbutic properties of certain food substances with guinea-pigs, it was observed that in those instances where pregnancy intervened the guinea-pigs presented a different picture than that of the usual fully developed scurvy. They did not become ill as soon as the nonpregnant animals of the same age, and the symptoms, such as swelling at the wrist, tenderness of the femurs, etc., were not nearly so severe. The difference was so definite and outstanding that we decided to make a special study of scurvy in a larger number of pregnant guinea-pigs, checked by control observations in nonpregnant scorbutic animals.

Our first effort, from March 15 to May 10, 1921, failed to produce an adequate number of pregnant guinea-pigs in a state of sufficiently advanced pregnancy and was unsuccessful in other respects.

A second attempt of this problem was not made until November, 1922. However, in the interim whenever we chanced to observe pregnancy in guinea-pigs during different types of scurvy experiments, we made records of the scorbutic picture in these individual cases. These animals, before being placed on a proscorbutic diet, always received a liberal supply of the best carrots and cabbages obtainable for table use. As no hindrance was set to the intake of these food substances, the guinea-pigs were free to partake, ad libitum, of the food rich in the water soluble vitamin C.

The cases observed by us in this manner simply reaffirmed our first observation. Various possible explanations of this finding were proposed and considered by us. Some seemed feasible for experimental study while others did not.

The following possibilities were considered:

1. Does the pregnant guinea-pig, as a result of pregnancy, eat much more of the antiscorbutic food than the nonpregnant animal?

2. Is the ability to store the antiscorbutic vitamin developed or increased as a result of pregnancy in the guinea-pig?

---

* Received for publication, June 10, 1924.
* Read before the Thirty-Sixth Annual Meeting of the American Pediatric Society, Pittsfield, Mass., June 5-7, 1924.
* From the Babies' Dispensary and Hospital and the Departments of Pediatrics of Lakeside Hospital and of the Medical School of Western Reserve University.

3. Is the growing embryo, as the sprouting pea or grain, able to produce the water soluble vitamin C and so protect itself and its mother?

4. Does pregnancy confer on the guinea-pig the ability to economize in the use of the water soluble vitamin C?

5. Does the increase in metabolism during pregnancy burn up deleterious products, which develop as the result of the absence of the water soluble vitamin C in the diet and which otherwise may be responsible for the advanced symptoms of scurvy?

6. Does the mother guinea-pig, as a result of pregnancy, possess a greater resistance to infections than does the nonpregnant guinea-pig, and is this conferred power responsible for the production of the milder picture of scurvy in the pregnant guinea-pig by the elimination or reduction of excessive secondary bacterial activity?

Obviously, the first and second possibilities are easier of attack than the others, and the first especially seemed a simple and plausible explanation. We, therefore, proceeded to determine whether the same mild picture of scurvy still would result if we limited the intake of a scorbutic food to a definitely measured amount, from the moment the females were exposed to the males up to a certain stage of pregnancy.

It was our opinion, based principally on the experiences obtained in the unsuccessful experiment referred to above, that pregnancy had to proceed to at least midterm if it were not to terminate in an abortion and so complicate observations. When premature cessation of pregnancy occurs the mother guinea-pig often will consume the fetus and so upset the experiment. Again it would be difficult, under these circumstances, to know positively the age of the fetus. And, finally, the effect of scurvy on the offspring could not be followed as well.

In order to ascertain, in addition, whether the size of the fetus or the weight of the total fetal mass played a rôle in molding the clinical picture of scurvy in the mother guinea-pig, we attempted to produce pregnancy of about four and of about six weeks' duration before stopping the intake of the antiscorbutic material. Another practical necessity for allowing pregnancy to proceed to a rather advanced stage was the difficulty of otherwise knowing with positiveness that pregnancy existed in the individual animal.

The antiscorbutic chosen was orange juice, and the dose administered was 5 c.c. of the fresh juice. The average weight of the animals was 500 gm., and 90 per cent. weighed close to this figure.

All of the guinea-pigs were fed on greens in our own laboratory for at least two weeks before the experiment was begun. When the administration of orange juice was started, all other antiscorbutic foods, such as carrots, cabbages, etc., were withheld. The animals were allowed to eat oats at will and in addition 50 c.c. of ordinary pasteurized

milk was offered daily. The cages were bedded with hay of one and the same lot.

All of the guinea-pigs were put on the orange juice diet on the same day. The males were placed with the females on the same day in the proportion of one male to five females. At the end of two weeks the males were removed and put back on greens, while the females, numbering forty-one, were continued on 5 c.c. of orange juice daily. At the end of four weeks the females were examined and it was found that about 50 per cent. were pregnant. Some of these were then placed on a proscorbutic diet, i. e., the 5 c.c. of orange juice was stopped, while the remainder were allowed to continue on the orange juice for another two weeks, making the total period of orange juice intake equal to eight weeks and the minimum stage of pregnancy, six weeks. The animals whose orange juice was stopped two weeks earlier, then, had received orange juice for a period of six weeks and were at least four weeks pregnant at the time of the beginning of the proscorbutic diet.

The 50 per cent. of the original group of females that did not become pregnant were continued on the orange juice and again exposed to the males. However, only a few became pregnant and the remainder, therefore, were put on a proscorbutic diet and used as controls.

Biweekly notes were made regarding the weight, symptoms and general condition of the guinea-pigs according to a key of from 1 + to 4 +. At death, necropsy was performed, and the findings recorded according to the same scheme.

As stated above, during the interim between the various attempts to produce an adequate number of pregnant guinea-pigs on a controlled water soluble vitamin C intake, pregnancies were observed in scorbutic guinea-pigs in the course of other experiments. A total of twenty-five of such pigs were studied. The records of their symptoms and necropsy findings served well as a comparative basis on which to estimate whether the 5 c.c. dose of orange juice, adopted by us for the group whose daily antiscorbutic intake was controlled, was liberal enough to meet the possibly increased demands of the pregnant pigs.

The sign of tenderness to pressure at the knee and wrist was eliminated early because it was found to be necessary to exert a rather strong degree of pressure, which, it was feared, in itself might produce local injury and complicate the interpretation.

The findings are shown in the tables and charts.

TABLE 1.—*Swelling Present at Wrists and Knees*

	Number Showing Swelling	Total Number in Group	Percentage of Group with Swelling
Pregnant	4	34	12
Controls	20	32	63

Table 1 indicates that swelling at the wrists and knees was found present in 63 per cent. of the control pigs and in only 12 per cent. of the pregnant pigs.

TABLE 2.—*Same as Table 1, Showing No Difference in the Control Guinea-Pigs in Swelling*

	Diet	Number Showing Swelling	Total Number in Group	Percentage of Group with Swelling
Pregnant	Greens	1	14	7
	Orange juice	3	20	15
Controls	Greens	7	11	63
	Orange juice	13	21	62

Table 2 brings out the same point as Table 1, and, in addition, shows that there is no difference in the control pigs as to the percentage of "swelling" observed, whether these control pigs received orange juice by hand or vegetables at will before being placed on a proscorbutic diet. In the pregnant pigs those on greens showed a smaller percentage of swelling than those on orange juice. The former group, however, is only two-thirds the size of the latter.

TABLE 3.—*Periods of Swelling Time*

	Days to Show Swelling	Number of Pigs	Total Number in Group
Pregnant	26	4	34
Controls	20	20	32

Table 3 indicates that it required a somewhat longer period of time for swelling at the wrists and knees to appear in the pregnant pigs, the few times it did appear in them, than in the control pigs.

TABLE 4.—*Comparison Between Live Born and Dead Born Guinea-Pigs*

Diet	Number of Mothers	Percentage of Mothers	Number of Fetuses	Condition	Percentage of Fetuses
Greens	4	30	7	Living	28
Greens	9	70	17	Dead	72
Orange juice	8*	32	11	Living	22
Orange juice	17*	68	38	Dead	78

* Included in this number are five mothers that produced both living and dead fetuses.

Table 4 shows that the percentage of dead born or live born pigs was approximately the same in both the spontaneously green fed group and in the hand fed orange juice group.

TABLE 5.—*Slightly Higher Percentage of Live Guinea-Pigs Produced by 8-Week Orange Juice Diet Than by 6-Week Orange Juice Diet*

Diet	Time, Weeks	Number of Mothers	Percentage of Mothers	No. of Fetuses Produced	Condition	Percentage
Orange juice.....	6	3*	27	3	Alive	20
	6	8*	73	12	Dead	80
	8	4†	40	6	Alive	27
	8	6†	60	16	Dead	73

* Included in this number are three mothers that produced both living and dead fetuses.
† Included in this number are two mothers that produced both living and dead fetuses.

Table 5 indicates that the pregnant guinea-pigs that received orange juice for eight weeks, prior to being placed on the proscorbutic diet, produced a slightly higher percentage of live animals and a slightly smaller percentage of dead animals than did the six week group. This finding indicates that the closer pregnancy is to full term the better are the chances for a live offspring.

TABLE 6.—*The Degrees of Scurvy Found at Necropsy in Fetuses*

Diagnosis	Degree	No. of Fetuses	Percentage	Percentage Totals	
Scurvy.....	4 plus	5	10	26	70
Scurvy.....	3 plus	4	8		
Scurvy.....	2 plus	4	8		
Scurvy.....	1 plus	21	44	74	
	Question	5	10		
Normal.....		10	20		30

Table 6 shows the degrees of scurvy as they were found in the fetuses at necropsy. Some of the pathologic findings were so severe as to be classified as 4 +. The majority, by far, however, were very mild. If the macroscopic necropsy diagnosis of the questionable and 1 + cases is considered too fine and these are, as a result, added to the normal, the amount of fetuses showing no changes or such that cannot be considered sufficient evidence in favor of scurvy would be 74 per cent. Twenty-six per cent., however, showed pathologic findings that must, without question, be called scorbutic in nature, at least from the macroscopic standpoint. If the 1 + cases are included in the positive group the percentage of scurvy in the fetuses is high, namely, 70 per cent.

TABLE 7.—*Degrees of Scurvy Found at Necropsy in Pregnant Scorbutic Guinea-Pigs and in Controls*

Necropsy—Control					Necropsy—Pregnant				
Scurvy	Number	Percentage			Scurvy	Number	Percentage		
4 plus	21	65.6	84.3	100	4 plus	6	17.6	38.3	70.6
3 plus	6	18.7			3 plus	7	20.7		
2 plus	5	15.7			2 plus	11	32.3		
1 plus	0	0.0			1 plus	6	17.6		
					Normal	4	11.8		

Table 7 gives the percentage of the various degrees of scurvy found at necropsy, in both the pregnant scorbutic guinea-pigs and in the non-pregnant controls, and indicates clearly the marked difference between the two groups.

Chart 1 shows the relative degree of the individual scorbutic lesions as they were found at necropsy in the pregnant scorbutic animals and in the controls. It is evident that the necropsy revealed a much milder scurvy to be present in the former than in the latter. The pregnant guinea-pigs at necropsy often still possessed a liberal layer of adipose tissue, whereas the control pigs did not.

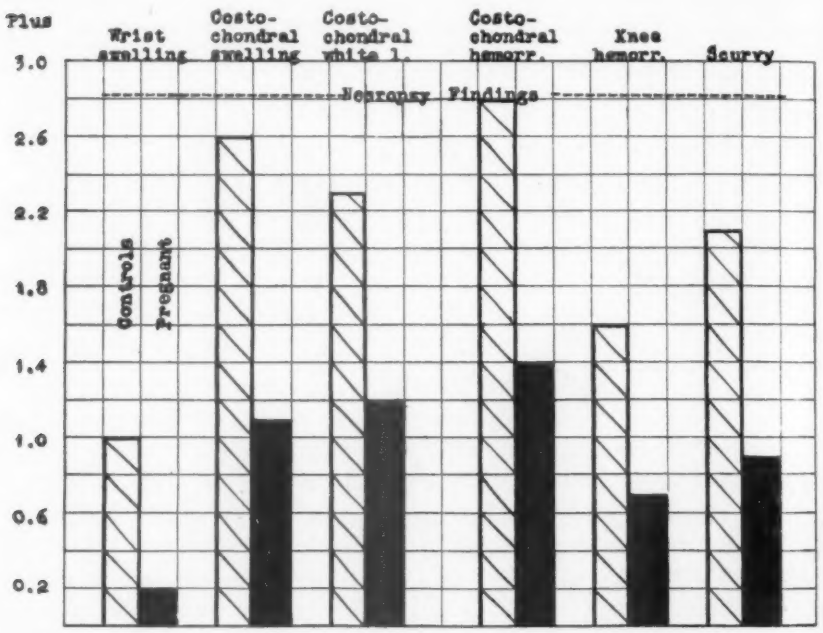

Chart 1.—The relative degree of the individual scorbutic lesions, found at necropsy in the pregnant scorbutic animals and in the controls.

Chart 2 shows a composite weight curve for two cases each, of both pregnant six week orange juice fed and eight week orange juice fed guinea-pigs and their corresponding controls. The term "Dead" indicates in the chart the time of death of the first pig of each group and the end of the curve line the time of the death of the second pig. It indicates how the pregnant animals continue to gain in weight at a time when the nonpregnant are stationary in weight or proceeding slowly downward. It shows further how abrupt and rapid, on the other hand, is the descent of the weight curve in the pregnant guinea-pig as soon as pregnancy has been terminated. And finally, it indicates that the time of death is about the same for both the nonpregnant and the pregnant

scorbutic guinea-pig, even though the clinical picture during life and the pathologic picture after death are so severe in the one and so mild in the other.

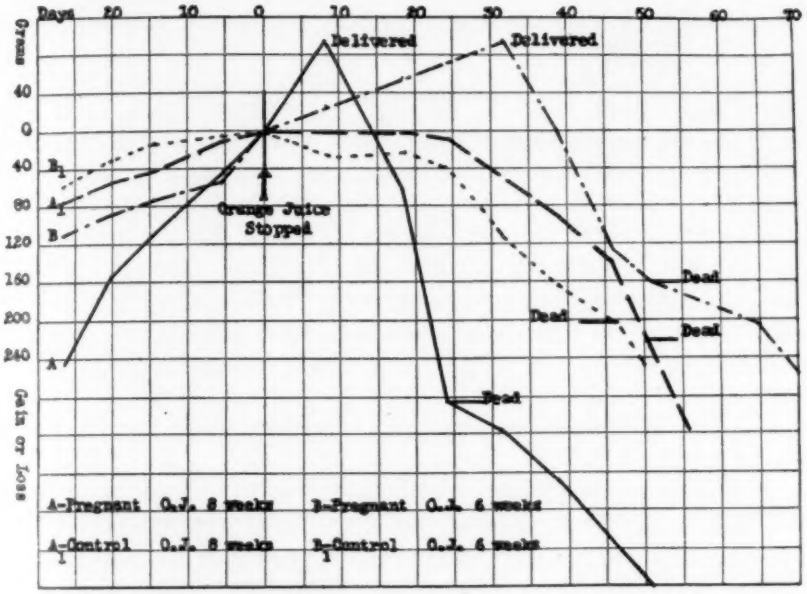

Chart 2.—A composite weight curve for two cases each, of both pregnant six and eight weeks orange juice fed guinea-pigs and their controls.

TABLE 8.—*Term of Life of Scorbutic Guinea-Pigs*

	Diet	Days Living After Anti-scorbutic Stopped
Pregnant	Greens	30
	Orange juice	31
Controls	Greens	31
	Orange juice	32

Table 8 presents, again, what has just been pointed out in Chart 2, namely, that the average term of life of the scorbutic guinea-pig, whether pregnant or nonpregnant, after the stopping of the antiscorbutic food is practically the same.

TABLE 9.—*Same as Table 8, and in Addition Shows That Orange Juice Does Not Prolong Life*

	Pregnant		Control	
Weeks on orange juice	6	8	6	8
Died after orange juice was stopped	36 days	27 days	33 days	32 days
Number of adults	8	8	3	4

Table 9 reiterates the conclusions of Table 8 and, in addition, shows that the extra two weeks of intake of orange juice in the pregnant pigs before being placed on the proscorbutic diet does not prolong life. Just the opposite really occurs; the mother pig seems to die sooner, possibly because the pregnancy is terminated earlier than in the six week orange juice fed animals.

COMMENT

That pregnancy modifies the picture of scurvy in guinea-pigs is evident in the first place by the postponing of the development of the supposedly characteristic active symptoms and, in the second place, by the lessening of their severity. Recently, Nobel [1] has reported similar observations on four pregnant and five nonpregnant scorbutic guinea-pigs. However, the necropsy findings, both macroscopic and microscopic, in three out of the four pregnant animals were negative, according to Erdheim, except for the presence of porotic changes, which Erdheim states are an integral part of the microscopic picture of scurvy but which, when present alone, cannot be considered characteristic of this disease.

Nobel, therefore, concludes that usually neither in the mother nor in the fetus can scurvy be produced, even though the proscorbutic diet during pregnancy continues for a period as long as thirty-nine days.

This conclusion of Nobel does not correspond with our own observations. In some of our cases, both in the mother and in the offspring, the changes found were so characteristic as to justify their being accepted as truly scorbutic. The difference in our findings may be explained by the fact that Nobel's guinea-pigs were much heavier than our own and were probably full grown. Also, his series was smaller, consisting of four animals. Observations on a larger group of the same type of guinea-pigs such as Nobel used might modify his findings. We are at present engaged in such a study on a larger scale.

In our own series, there is no appreciable difference to be made out between the pregnant scorbutic guinea-pigs that fed themselves on greens during pregnancy up to the time of being placed on a proscorbutic diet and the pregnant scorbutic animals that received from us, by hand, 5 c.c. of orange juice daily. In other words, 5 c.c. of orange juice gives to the pregnant guinea-pigs an adequate supply of antiscorbutic material. On the other hand, the dose of 5 c.c. of orange juice for a pregnant animal can hardly be considered excessive when it is generally accepted that 3 c.c. of orange juice is necessary to insure growth and freedom from scorbutic symptoms in the ordinary guinea-pig. It does seem probable from our experience that pregnancy does not stimulate the guinea-pig to ingest an excessive amount of antiscorbutic substance.

1. Nobel, E.: Ztschr. f. d. ges. Exper. Med. **38**:528, 1923.

Likewise, it seems to us to indicate that in all probability the pregnant guinea-pig does not store the antiscorbutic substance in larger quantities than does the nonpregnant animal. This idea also seems to be borne out by the finding that the giving of orange juice to some of the pregnant guinea-pigs for a period of eight weeks did not give these animals, for their life continuation, an advantage over the pregnant guinea-pigs receiving the orange juice for a period of six weeks. Likewise, the rapid decline to death after pregnancy is ended speaks against the presence in the body of the mother guinea-pig of a large storage of antiscorbutic vitamin. Nobel's animals, even though they were free from the characteristic symptoms of scurvy, collapsed and died as quickly after parturition as did our own.

It is a strange thing that these animals should present a relatively mild picture of scurvy and still die, on the average, within the same space of time as do the nonpregnant guinea-pigs who develop what is accepted to be a severe type of scurvy. Why do these guinea-pig mothers die so quickly even though their scorbutic symptoms are, relatively speaking, so mild? Do they die, even though the clinical and pathologic picture is so different from that seen in the nonpregnant scorbutic guinea-pigs, because of the continued absence of the water soluble vitamin C in the diet or do they die because of other dietetic deficiencies, such as an inadequate intake of protein or of the water soluble vitamin B? We have, in the course of other work, fed to guinea-pigs, after they had developed scurvy, liberal amounts of the water soluble vitamin B without obtaining any beneficial or postponing effect on the picture of the scurvy. On the contrary, this particular group of pigs seemed to proceed to death with greater speed than is ordinarily the case.

There is a growing feeling in some quarters, both here and abroad, as expressed by Abels,[2] Meyer[3] and Hess,[4] that the symptoms of the advanced and active stage of scurvy are, to a large degree, secondary symptoms produced by bacterial activity, made possible by the production of a state of dysergy in the animal organism as a result of the absence of an adequate amount of the water soluble vitamin C in the diet.

It is a common experience to see frail and normal women, who are not extremely overworked, thrive especially well during pregnancy. Might it not be that the proscorbutic diet does not produce the typical scurvy in the pregnant guinea-pig because pregnancy possibly raises the resistance of the mother animal to bacterial invasion. If this is so, the

2. Abels, H.: Die skorbutische Dysergie, Ztschr. f. Kinder. **36**:295, 1923.
3. Meyer, L. F.: Die skorbutische Diathese, Monatschr. f. Kinderh. **25**: 454, 1923.
4. Hess, A. F.: Nutritional Disorders, Boston M. & S. J. **187**:101, 1922.

mother guinea-pig may still die as the result of scurvy, if by scurvy we mean any pathologic condition that is due to the inadequate intake of the antiscorbutic vitamin, even though the clinical picture at death is mild as compared with the ordinary cases of scurvy that we see. If this condition of affairs really obtains, then we shall have to conclude that the picture of scurvy, as we see it in its active and advanced form, is due to the direct action of the deficit in water soluble vitamin C and also to the indirect action of bacteria which operate if the direct injury has prepared the way for them.

The suggestion that the fetus may be able to produce the antiscorbutic vitamin, as does the sprouting grain, is most alluring. However, no evidence of any member of the animal kingdom being able to synthesize the water soluble vitamin C, as are members of the vegetable kingdom, has been brought forward. The rat, it is true, does not develop scurvy, but this may be due to other conditions than to an ability to synthesize the vitamin. One would think that, if the relative freedom from the severe symptoms of scurvy were due to the production of water soluble vitamin C by the fetus, the mother guinea-pig would live longer after parturition and would develop a severer form of scurvy, just as do the nonpregnant scorbutic animals.

CONCLUSIONS

1. Pregnancy modifies both the clinical and pathologic picture of scurvy in guinea-pigs. The symptoms accepted at present to be characteristic of advanced scurvy are entirely absent or appear much later, and are much less severe than in nonpregnant guinea-pigs.

2. The daily intake of 5 c.c. of fresh orange juice supplies to the pregnant guinea-pigs, of an average weight of 500 gm., at least as much antiscorbutic material as these animals will consume of their own accord when free to feed on greens.

3. The life term of the pregnant scorbutic guinea-pigs on a proscorbutic diet is, on the average, the same as that of the controls, even though the clinical and pathologic picture of scurvy is mild in the former and severe in the latter.

4. It is suggested that probably the change in the picture of scurvy in pregnant guinea-pigs is due to the changed metabolic conditions produced by pregnancy, which either raise the resistance of the animal to infections or enable it to economize in the use of the antiscorbutic vitamin.

5. It is suggested that, even though symptoms of scurvy in the pregnant guinea-pig are milder in degree, the animal's death after parturition is, nevertheless, due to the inadequate intake of the antiscorbutic vitamin.

FOREIGN BODIES IN THE AIR AND FOOD PASSAGES OF INFANTS AND CHILDREN, WITH ESPECIAL REFERENCE TO THE CLINICAL DIAGNOSIS *

RUSSELL S. ROWLAND, M.D.
DETROIT

It is difficult to determine the frequency of foreign bodies in the air and food passages in general, however it is safe to say that this condition is more common than many suppose. Such foreign body cases have occurred in my own practice more often than those with either typhoid fever or diabetes. In an analysis of a large series Graham [1] finds that 66 per cent., or approximately two-thirds of all foreign bodies in the air and food passages, occur in infants and children. The bad habit of putting objects into the mouth accounts for most of these accidents. The pediatrician cannot warn parents too frequently of this danger because, as Jackson [2] states, nearly 90 per cent. of the foreign intruders are due to carelessness that is avoidable. Because of the nature of the treatment and the seriousness of these accidents, the diagnosis is most important.

The diagnosis of foreign bodies in the air and food passages rests on the history, the physical signs and symptoms, and the roentgen-ray and endoscopic examinations. The object of this paper is to stress the importance of the history, symptoms and physical signs; in other words, the *clinical diagnosis* as well as the study by roentgen ray and endoscopy in every suspected foreign body case. Jackson [3] says that the roentgen ray is the most valuable single aid in diagnosis, but that a careful physical examination should always be made first. In many instances it is only by seeking the history and studying the signs and symptoms that an early diagnosis, frequently so essential to successful surgical treatment, can be made. McCrae [4] finds that from 10 to 15 per cent. of all such foreign bodies cannot be demonstrated by roentgen ray. In such patients the physical examination is of the utmost importance, and the diagnosis should be completed by an endoscopic examination.

---

* Received for publication, May 15, 1924.

* Originally presented as a lantern slide demonstration before the Central States Pediatric Society, Oct. 18, 1923.

1. Graham, E. E.: Foreign Bodies in the Air and Food Passages, Am. J. Dis. Child. **19**:119 (Feb.) 1920.

2. Jackson, Chevalier: What Does Your Baby Put in His Mouth? Hygeia **1**:561 (Dec.) 1923.

3. Jackson, Chevalier: The Symptomatology and Diagnosis of Foreign Bodies in the Air and Food Passages, Am. J. M. Sc. **161**:605 (May) 1921.

4. McCrae, Thomas: The Physical Signs of Foreign Bodies in the Bronchi, Am. J. M. Sc. **159**:313 (March) 1920.

A number of pathologic conditions may be confused with foreign bodies in the air and food passages. Diphtheria has been diagnosed when a foreign body was present, so also a foreign body has been diagnosed as diphtheria. Anaphylactic asthma and thymic asthma have been diagnosed when a foreign body was the etiologic factor. McRae distinguishes between two classes of unrecognized foreign body cases: (1) very acute cases, usually following the aspiration of an organic body like a peanut, in which the sudden onset with fever and respiratory tract symptoms suggests pneumonia; (2) chronic cases, due mostly to metallic bodies, in which a diagnosis of tuberculosis or bronchiectasis has been made.

For the convenience in the study of foreign bodies in the air and food passages, four groups may be considered: (*a*) patients with a clear history of having aspirated a foreign body and showing typical signs and symptoms, the most frequent type; (*b*) patients with symptoms suggesting the possibility of a foreign body, in which no history can be obtained, of not infrequent occurrence; (*c*) less often, patients in which there is no history, the signs and symptoms are very slight, and a foreign body is accidentally discovered during a routine examination, including the roentgen ray; (*d*) and finally, cases of obscure pulmonary involvement, which with a better knowledge and more careful consideration of the history signs and symptoms might be correctly recognized as foreign body cases.

These groups may further be classified into acute and chronic, partially obstructive and completely obstructive. The bodies themselves may be radio-opaque, usually metal or bone; nonradio-opaque, mostly organic objects, such as nut kernels, seeds, food particles and nursery powders. In this paper the foregoing groupings and the sequence of trachea, esophagus, stomach, bronchi and lungs will be followed.

TRACHEAL AND INTESTINAL TRACT CASES

Foreign bodies, when arrested in the pharynx, larynx or trachea most often give a definite history and produce marked symptoms. They are consequently emergencies and usually are referred directly to the surgeon for treatment. This is not always true, especially in infants and little children with foreign bodies in the trachea, as in such patients the initial symptoms frequently may not be noticed or are forgotten. There is a symptomless period and then the tracheal symptoms develop. Such bodies are usually movable and their movements can often be felt by the patient. The cough may be continuous and so violent as to induce vomiting. The sudden shutting off of the expiratory blast and the phonation during paroxysmal cough is very characteristic. An audible slap and a palpable thud are pathognomonic. Asthmatoid wheeze is usually present and is often louder and of lower pitch than the asthmatoid wheeze of bronchial foreign bodies.

CASE 1.—*Typical case with a clear history, definite symptoms and roentgen-ray findings, in which the diagnosis could hardly be in doubt.* M. W., a girl, aged 2 years and 2 months, had a safety pin in the trachea. The patient choked and strangled and became immediately quite cyanotic and breathed with difficulty. There was a persistent cough which became croupy. Between choking spells there was a loud wheezy respiration and evident signs of pain and distress.

The position of the foreign body in this case, as shown in the roentgen-ray plate, should be remembered in relation to the next case. The foreign body lay in the saggital plane with its edge pointing out-

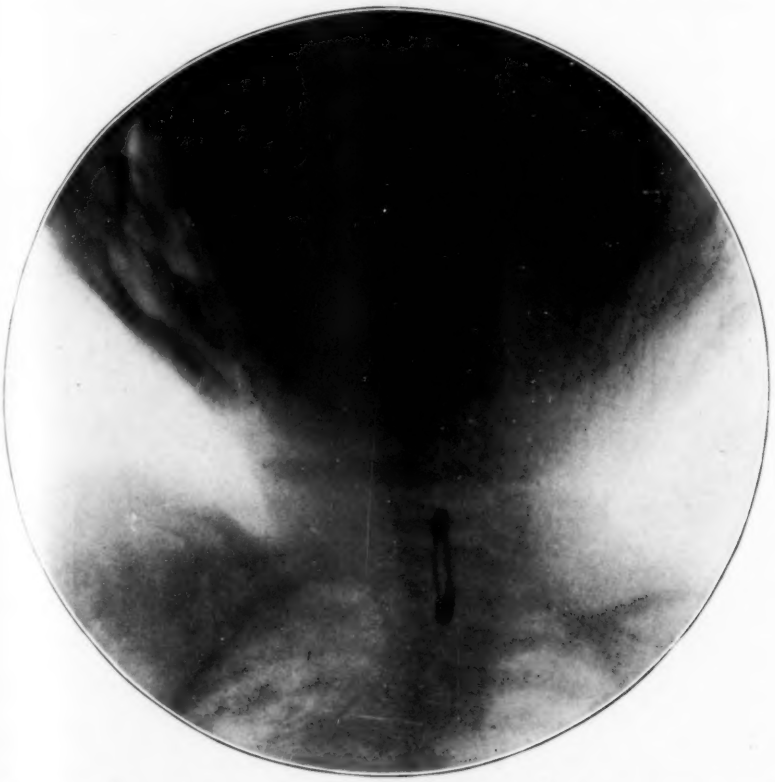

Fig. 1 (Case 1).—M. W., aged 2 years and 2 months, with a safety pin in the trachea.

ward, as do all flat elliptical bodies in the trachea. This is because it passes through the anteroposterior glottic chink into the trachea, the posterior wall of which is flexible.

CASE 2.—Safety pin in the esophagus. In this case the foreign object lay flat because the esophagus is a flattened tube, due to pressure from the structures in front and behind it.

The above facts are important, as even with roentgen-ray plates foreign bodies have been supposed to be in the trachea when they really were in the esophagus, and tracheotomy has been performed.

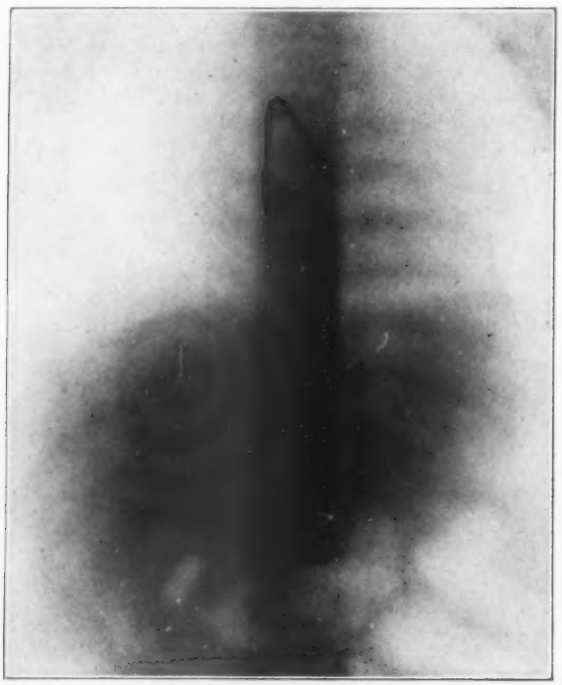

Fig. 2 (Case 2).—An infant with a safety pin in the esophagus.

Fig. 3 (Case 3).—E. G., aged 4 months. An anteroposterior view of a large collar button in the esophagus.

CASE 3.—*A case with no history and very few symptoms.* E. G., an infant, aged 4 months, had a large collar button in the esophagus. The mother noticed that her baby, from the age of 2 months, often choked when nursing, especially if she was allowed to nurse quickly. This was not considered serious as she gained normally and seemed happy in every way. Her cry was clear and lusty. When 4 four months old, she began to cough and had a slight elevation of temperature. Ten days later she became much worse. The temperature rose to 104, the respirations were rapid. There was a severe laryngeal cough, a husky cry and she choked when fed. Examination at this time suggested bronchopneumonia on both sides, which was believed to account for all the symptoms.

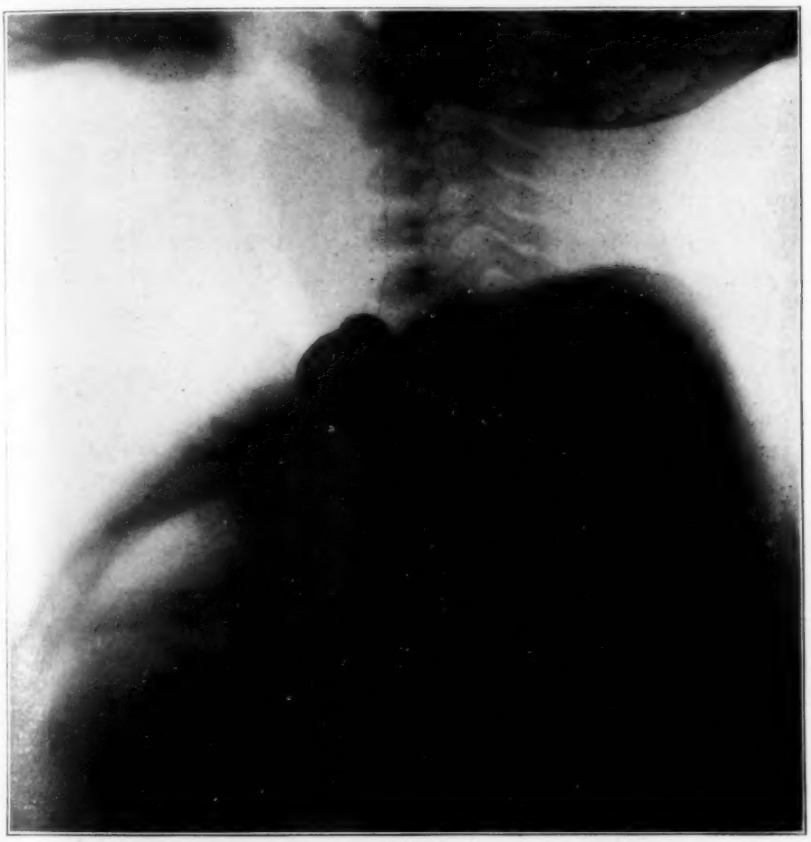

Fig. 4 (Case 3).—Lateral view, the same patient.

Two weeks later the acute symptoms subsided, but as the difficulty in feeding persisted, a roentgen-ray examination was made, which showed a collar button lying flat in the esophagus, the enlarged ends wrapped around the trachea and considerable inflammatory change involving the adjacent parts. The foreign body had produced so much damage that it could not be removed from above. It was finally removed through an external incision of the neck. The baby died.

Sometimes there is no history and there are no diagnostic symptoms of foreign bodies in the esophagus. At other times, food may be swallowed easily and regurgitated, or swallowed with difficulty as in the case

of stricture. Fluids may be taken when solid food will not pass. Even, as in this case, a stomach tube may be introduced without discovering the foreign body. With such symptoms persisting without an explanation, a roentgen-ray examination should be made, as only an early diagnosis will save the patient from the ill effects of pressure, which in the above case produced ulceration even through into the trachea. For the same reason in cases of this kind it is not safe to allow foreign bodies which have lodged in the esophagus to remain for any length of time. Bones, with adherent tissue, decompose rapidly and are especially inclined to cause local inflammation.

CASE 4.—Safety pin in the stomach. Here there was a definite history of choking and swallowing a safety pin. This patient is mentioned because the foreign body remained in the stomach over six months without signs or symptoms. The case was observed by roentgen ray. There were no diagnostic signs and symptoms of foreign bodies in the stomach.

FOREIGN BODIES IN THE BRONCHI AND LUNGS

Of most interest to the pediatritian from a diagnostic point of view are patients with foreign bodies in the bronchi and lungs, especially the nonradio-opaque type.

If one wished to test out his skill in physical diagnosis, I venture to say no better material for study could be found than one of these obscure cases. Jackson [5] has recently published a very illuminating article on "The Mechanism of Physical Signs With Especial Reference to Foreign Bodies in the Bronchi." He explains clearly the reasons for multiplicity and changeability of signs and symptoms. There are three factors involved: (1) the bronchial movements; (2) the presence, absence or shifting of secretions, and (3) the presence and movements of the foreign bodies. He also shows that foreign bodies have a tendency to reach the bronchi supplying the lower lobes, and are more often on the right side. This is because objects lower by gravity, and the right main bronchus is larger than the left, and is more in direct line with the trachea.

McCrae,[4] in discussing this subject, mentions three important diagnostic points:

1. Decreased expansion of the affected side, which he says is the only sign that occurs in every patient, and may be the only sign present. He mentions an illustrative case in this connection, with a history of having aspirated a safety pin, in which there were no other signs or symptoms. The roentgenogram showed an open safety pin in the left bronchus without any evidence of inflammatory change in the lungs.

---

5. Jackson, Chevalier: The Mechanism of Physical Signs, with Especial Reference to Foreign Bodies in the Bronchi, Am. J. M. Sc. **165**:313 (March) 1923.

2. "Tissue paper râles." These râles he described as finer and softer than the early crackling râles heard in lobar pneumonia. They occur at the end of inspiration, are more marked on deep breathing and give the impression of coming from a distance. They are difficult to hear, and so far have only been heard with metallic objects. It is because they are localized in the region of the foreign body that they are of especial value.

3. "Asthmatoid wheeze." This sign, originally discussed by Jackson,[6] is of considerable importance, particularly in cases where the foreign body does not show by means of the roentgen-ray examination. It should be listened for in all cases where the presence of a foreign body has to be considered. This sound can be heard by placing the bell of the stethoscope close to the patient's mouth. It may be heard both on inspiration and expiration, but sometimes is only audible at the end of expiration. Forcible respiratory effort usually increases the loudness and intensity. It differs from the wheezing sound heard with bronchial asthma but the difference is difficult to describe. The wheeze varies in pitch and loudness depending on the character of the foreign body causing it. It can never be heard over the chest wall. In some cases it comes and goes without any explanation being evident.

The following group represents a series of cases of organic foreign bodies in the bronchi. They are not demonstrable by roentgen ray but they frequently give a striking roentgen-ray picture and quite characteristic signs and symptoms.

Case 5.—*No positive physical signs or roentgen-ray finding until five weeks after the accident.*—Baby B., a boy, aged 22 months, had a peanut in the right lower bronchus. The patient attempted to swallow some peanuts. Immediately he was taken with a choking spell and difficult breathing, accompanied by wheezing. The father, a hay fever sufferer, was experiencing an attack at this time, and it was assumed for this reason that the patient had an attack of anaphylactic asthma. There was little subjective discomfort, and only moderately severe dyspnea. The wheeze became most pronounced at night. As the respiratory symptoms did not disappear, a foreign body was considered, and a roentgen-ray examination was made five weeks after the onset, showing the striking findings of nonradio-opaque foreign bodies. Following this, a small irregular portion of peanut was removed from the right secondary bronchus.

The failure to make an earlier diagnosis was due to the fact that sufficient importance was not attached to the peanut swallowing episode, which was considered merely as a matter of coincidence, the family history of anaphylactic asthma, the almost complete absence of subjective symptoms; the failure to differentiate between asthmatoid wheeze and the simple asthmatic dyspnea.

The signs and symptoms in the above case were not pronounced because the object was small and not obstructive when the examinations were made, and did not cause local irritation. It happens often that in little children such bodies are completely obstructive and then the

6. Jackson, Chevalier: A New Diagnostic Sign of Foreign Body in Trachea or Bronchi, the "Asthmatoid Wheeze," Am. J. M. Sc. **156**:625 (Nov.) 1918.

bronchial secretions are considerably increased and difficult to expel. In such patients the symptoms are much more severe and a diffuse purulent tracheobronchitis, which Jackson and Spencer [7] first described under the name of arachidic (peanut) bronchitis, develops.

In this condition there is a sudden onset with high temperature, dyspnea, cyanosis and a paroxysmal cough, the picture is one of a severe toxemia. The child is unable to cough up the thick secretions through the swollen passages and "drowns in its own secretions."

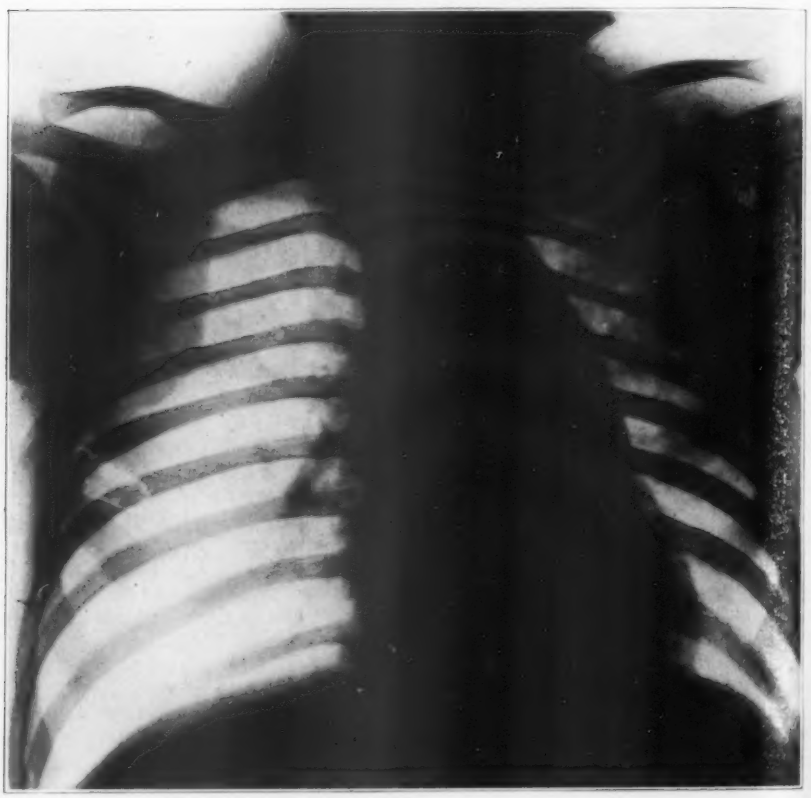

Fig. 5 (Case 5).—B., aged 22 months, with a peanut in the right lower bronchus.

In the early stage an acute obstructive emphysema is present distal to the foreign body, manifest by limited expansion, muffled tympanic percussion, diminished or absent breath sounds on the obstructed side, many râles and harsh breathing on the free side.

---

7. Jackson, Chevalier, and Spencer, W. H.: Arachidic Bronchitis, J. A. M. A. **73**:672 (Aug. 30) 1919.

Radiography confirms these signs by showing (see Fig. 5), (1) greater transparency on the obstructed side, (2) displacement of the mediastinal contents toward the free side and (3) depression and limitation of the diaphragmatic movements on the obstructed side.

CASE 6.—*Rapid onset and severe toxic symptoms give the picture of Jackson's arachidic bronchitis.* Baby R. C., a boy, aged 8 months, had a piece of cork in the right lower bronchus.

The patient had a severe choking spell while playing with a thermos bottle cork. Almost immediately he became cyanotic, weak and limp. Similar spells alternated, with periods of labored wheezy breathing. The temperature rose rapidly to nearly 104, the pulse was increased in rate and weak. When I was called to see him about thirty-six hours later, because it was thought pneumonia might have developed, he was in a state of collapse. The breathing was labored, there was a rather loud asthmatoid wheeze, and considerable secretion in the throat. Examination showed decreased expansion on the right side with diminished resonance at the base, hyperresonance over the upper portion of the chest, and numerous moist râles low down in the back. Throughout the left chest there was harsh breathing and scattered coarse râles.

This patient is of interest because there was a fairly definite history, symptoms and signs characteristic of arachidic bronchitis. Ipecac had been given to remove the foreign body, an absurd and dangerous procedure. The roentgen-ray examination was not made until just before the endoscopic examination, because it was not known at this time that such a nonradio-opaque foreign body could be diagnosed in that way. The roentgen-ray plates gave the usual evidences of nonradio-opaque foreign bodies. After an apparently fruitless search the bronchoscope was withdrawn, and the piece of cork was found impacted in the end of the bronchoscope.

CASE 7.—(Same symptoms as Case 6). Baby C., aged 16 months, had nut kernels in the bronchi on both sides. The patient had a history of suddenly strangling and becoming weak and cyanotic. Following the initial attack, which lasted about one-half hour, the respirations were very rapid and superficial. The choking spell recurred frequently. There were periods of restlessness and distress, considerable dyspnea and a loud wheeze. In the evening the temperature rose to 103, the pulse was rapid and weak and toxic symptoms developed. On the following day the temperature reached 105.

Physical examination showed the chest expanded, with rapid superficial respiratory movements. The percussion note was tympanitic, except for slightly diminished resonance low down on the left side. The breathing over this area was faint and distant. Over the rest of the chest the respirations were loud and harsh, and there were many coarse râles and rhonchi throughout both sides. The patient died on the fourth day. Diagnosis: Arachidic bronchitis, due to nut kernels in bronchi on both sides.

The hospital entrance diagnosis was bronchopneumonia, but the physical signs and symptoms should have excited a suspicion of foreign body. Endoscopic examination revealed pieces of nut kernel in bronchi on both sides. The case is of further interest because the foreign bodies were on both sides.

Cases 8 and 9 emphasize the importance of the physical signs, as the roentgen-ray reports were negative both for direct and indirect evidence of a foreign body.

It should be mentioned in this connection that advances in roentgen-ray technic and interpretation are bringing the clinical and roentgen-ray findings in closer accord. While the roentgen-ray reports were negative, we believe from our study that these plates do show the indirect evidence of nonradio-opaque foreign bodies.

With the consent of Dr. W. A. Evans, the films and my record of Cases 8, 9 and 10 were submitted to Dr. W. T. Manges of Philadelphia, who is the present roentgen-ray authority on this subject. As his statements confirm my own opinions and as his explanations contain so much of value for those who are doing their own fluoroscopic and roentgen-ray work, with a few minor changes and omissions they have been included in this report. His study of these films cannot but impress the importance of the clinical findings, in association with a correct

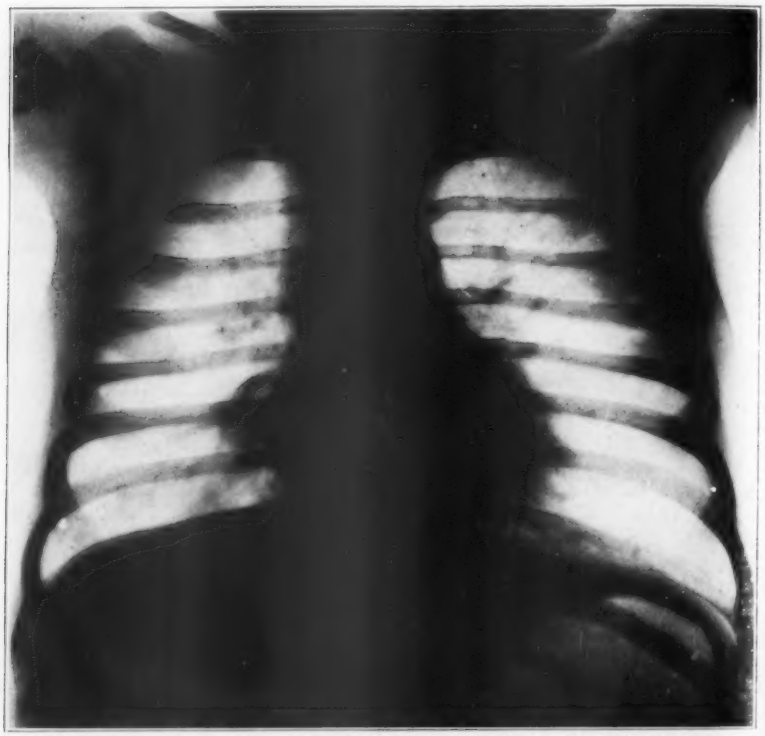

Fig. 6 (Case 7).—C., aged 16 months, with nut shells in bronchi in both sides.

roentgen-ray interpretation in the diagnosis of nonradio-opaque foreign bodies in the bronchi, as even with these careful roentgen-ray analyses the clinical findings are necessary to complete the diagnosis.

ROENTGEN-RAY REPORT

Dr. Manges first makes the general statement that it is somewhat difficult to tell about nonopaque foreign bodies, unless the films are made with an exceedingly short exposure and at inspiration and especially at the end of expiration. A single exposure at inspiration might show a perfectly normal chest, even though there was obstructive emphysema on one side, for the simple reason that as a rule there is compensatory emphysema on the opposite side. This means, of course, that at the end of inspiration the two lungs have prac-

tically the same appearance. . . . In conclusion he says: From the films that you have sent, one would not be justified in making a diagnosis of foreign body without a history of aspiration, and I again want to impress on you that you must make your exposures both at inspiration and at expiration, and that the fluoroscopic examination is an extremely important part of the study because you are never certain that your exposures are made at full inspiration and full expiration. And, further, that if the foreign body is in the trachea and producing expiratory obstruction, the signs of obstructive emphysema are present in both lungs.

Dr. Manges' discussion of the individual cases has been inserted for convenience at the end of my own report in each case.

Case 8.—A. N., a boy, aged 3 years, had a portion of a nut kernel (pecan) completely obstructing the orifice of the left upper bronchus. When seen twenty-four hours before the operation, the bronchus probably was not completely obstructed.

The patient strangled during a crying spell while chewing pecan nuts. There was considerable distress with choking, lasting about fifteen minutes. This was followed by restful sleep and breathing without embarrassment, but with a pronounced wheeze which could be heard across the room. On the following day there were no abnormal findings except sibilant and moist râles heard over the entire chest. There was no discomfort, no embarrassment of breathing and no cough. Roentgen-ray examination on the second day resulted in a negative report for a foreign body. On the fourth day the wheeze became less pronounced and on the fifth day was not noticeable. It was thought at this time that the trouble was anaphylactic asthma, and the father, who is a physician, ceased to worry about a foreign body. Quite suddenly, on the afternoon of the seventh day, the breathing became rapid and the patient appeared distressed, grunting with almost every expiration. In the evening the temperature rose to 102, and the pulse became correspondingly rapid. There was marked decreased expansion of the left chest with retraction of the lower intercostal spaces. The breath sounds were absent on the left side both anteriorly and posteriorly, and there was diminished resonance. The breath sounds over the right chest were tympanitic. On the following day the dulness on the left side was more pronounced and there was very little movement of the left chest. The temperature continued to climb, reaching from 103 to 105 degrees. The respirations were very rapid. The patient became toxic and vomited several times during the day and refused even fluids. With the above signs and symptoms, the roentgen-ray report on the eighth day was negative for a foreign body. We, however, believed the plates showed the indirect evidences of a foreign body on the left side.

Dr. Manges' Interpretation of Fig. 7.—It is difficult to determine anything definite from the film which you sent. It shows evidence of exudate collecting in the left lower lobe, with slightly increased transparency of the left upper lobe. The density in the left lower lobe, of course, indicates some sort of pathologic process associated either with a collection of exudate or with collapse of certain portions of the left lower lobe. The left diaphragm is slightly higher than the right, which leads me to believe that this exposure was made at full inspiration. On the following day, this youth was examined at the Jefferson Hospital by Dr. Cohen, one of my assistants. His report was: Marked obstructive emphysema in both the upper and lower lobes on the left side and compensatory emphysema on the right side. There was inflammatory pathology at the left base and there was evidence of obstruction of the left bronchus.

Diagnosis: Arachidic bronchitis due to nut kernels, completely obstructing the orifice of the left upper bronchus. The fact that the foreign body was on the left side is also of interest for reasons already stated, that foreign bodies more often lodge on the right side.

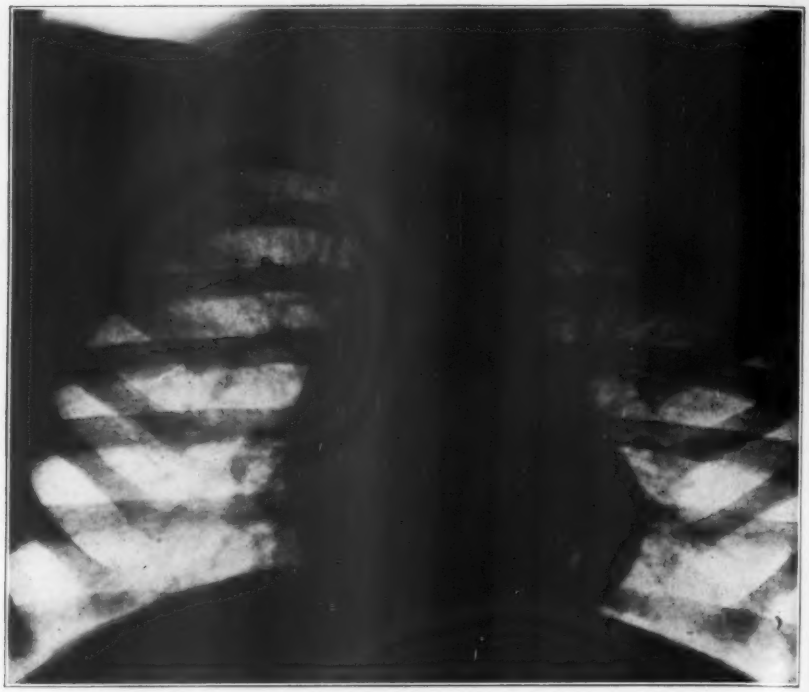

Fig. 7 (Case 8).—A. N., a boy, aged 3 years. Portions of nut kernel completely obstructing the orifice of the left upper bronchus.

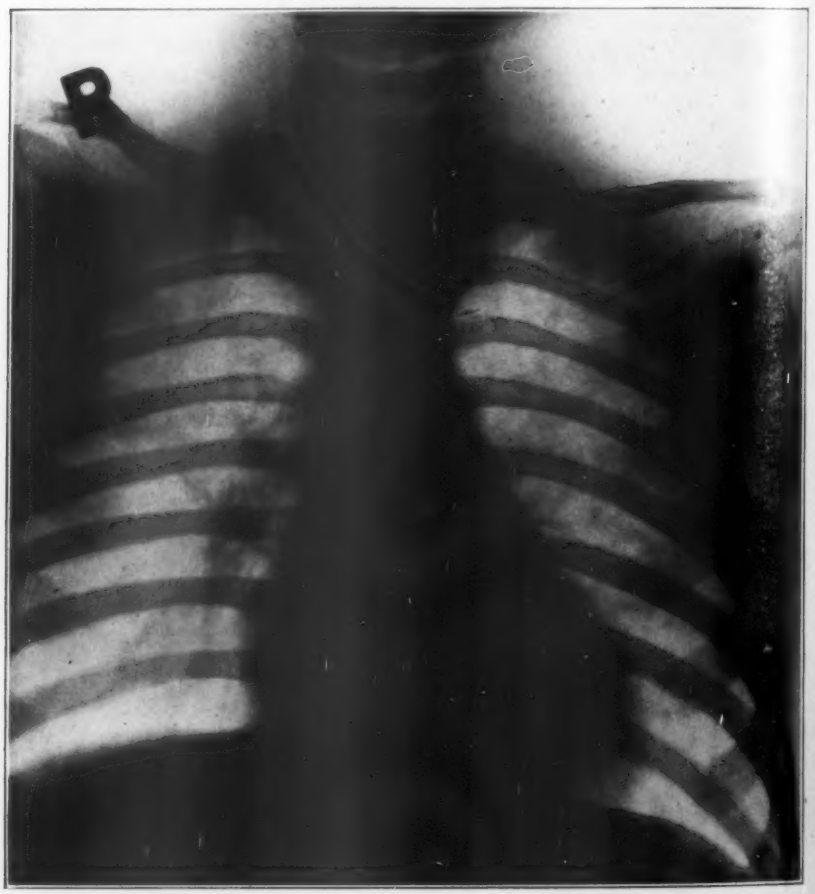

Fig. 8 (Case 9).—L. W., a girl, aged 14 months, had a nut kernel in the right main bronchus.

CASE 9.—L. W., a girl, aged 14 months, had a nut kerned (almond) in the right main bronchus.

The patient, while eating a piece of chocolate candy containing almonds, suddenly choked and strangled. She appeared to be in distress, became dyspneic but not cyanotic. After one night of restlessness there was a period of about two weeks with very few symptoms. There was a slight cough, no difficulty in eating and no vomiting. She appeared happy and showed no discomfort. Coincident with the onset of a coryza on the seventeenth day after the accident, she had a severe choking spell followed by a cough and croupy symptoms. She now appeared distressed at times, was quite hoarse and developed a wheeze. There was moderate dyspnea with occasionally a little cyanosis during choking spells.

When first observed on the following day she was slightly croupy and had a definite wheeze. Examination of the chest showed decreased expansion on the right side with marked retraction of the lower intercostal spaces. The left side appeared expanded and moved more with the respirations. There was good resonance over the upper portion of the right side, and diminished resonance below, especially in the right axilla. The percussion note was tympanitic over the entire left side. Auscultation showed coarse râles and rhonchi throughout both lungs, and an area of moist bubbling râles below and inside the angle of the right scapula.

On the following day, just before endoscopy was performed, it was very difficult to detect any difference on the two sides. There was a slight decreased expansion with retraction of the lower intercostal spaces on the right side. The area of dulness had disappeared, and the râles in the back were less numerous. The breath sounds were louder on the left side. This change was probably due to shifting of the foreign body.

The endoscopic examination showed a movable nut kernel in the right main bronchus.

Roentgen-ray plates on the day following the accident gave no evidence of a foreign body. Roentgen-ray report on the eighteenth day (Fig. 8) was still negative for foreign body. There was possibly a slight increased air penetration on the right side.

Dr. Manges' Interpretation of Fig. 8.—The film that you have sent me permits of a diagnosis, in view of the history, because it is perfectly clear that there is increased transparency of the right lower and middle lobes, and that the heart is perhaps slightly displaced to the left. I have no doubt that this exposure was made at the end of practically full inspiration because the diaphragms are in their normal relations. If you had observed this baby at the fluoroscope, you would have noticed that during the breathing cycle the heart would have moved from side to side and would have gone into the left chest during expiration and come toward the right more during inspiration. You would have noticed limitation of motion in the right diaphragm, with probably more than the normal motion in the left diaphragm. You would have noticed that the right lower lobe did not empty its share nearly as readily as the rest of the lung during expiration. I would have been led from this film alone to suggest the possibility of foreign body but would certainly not be willing to make a positive diagnosis from it.

OBSCURE CASES WITH NO POSITIVE DIAGNOSIS

As previously mentioned there are cases, doubtless, of obscure pulmonary involvement, which with a better knowledge of signs and symptoms might be correctly recognized as foreign body cases. The following case illustrates this point. Asthma and foreign body, as well as bronchopneumonia, were considered.

Case 10.—Baby W., aged 13 months, was one of twins, the other twin being well at the time of this illness. The onset was sudden with fever, croupy cough and a loud wheeze. The patient was dyspneic and had moderate cyanosis. Repeated cultures for diphtheria were negative, nevertheless, 10,000 units of antitoxin were given. The croupy symptoms were not relieved by steaming, local applications and an expectorant mixture. The temperature continued elevated, ranging to 103, and the loud wheeze persisted. There was considerable laryngeal secretion.

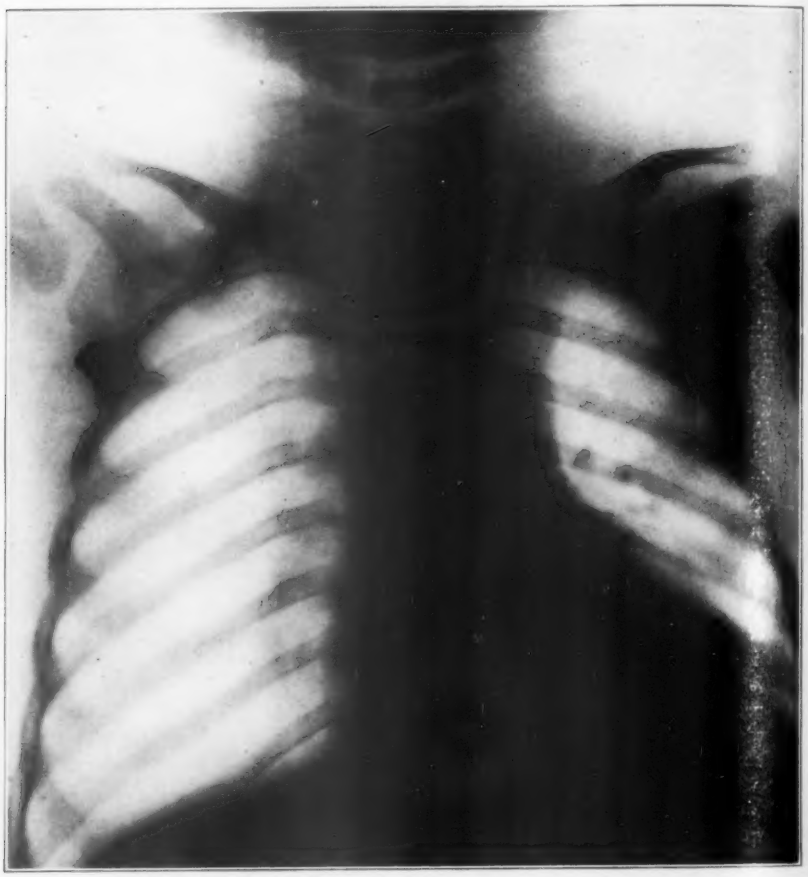

Fig. 9 (Case 10).—W., aged 13 months. An obscure case with no positive diagnosis.

On examination we suspected delayed expansion on the right side but could not be positive. The percussion was dull over the middle portion of the right side anteriorly and posteriorly, and hyperresonant over the upper portion. The breathing was distant and faint. There were more medium moist râles over the area of dulness on the right.

The roentgenogram suggested displacement of the mediastinal contents toward the left, and increased air penetration on the right. A lowering and flattening of the right leaf of the diaphragm (compare Figs. 9 and 5). A wide shadow above the cardiac area extending to the left was thought to be due to displacement of an enlarged thymus. There was no evidence of bronchopneumonia or other pulmonary infection.

No history could be obtained of having aspirated a foreign body. The symptoms and signs, as well as the roentgen-ray findings, were suggestive of partial obstruction of the right main bronchus. After consideration of these facts we believed that we had been dealing with a foreign body complicating status lymphaticus with asthmatic symptoms. The patient died. Necropsy was not permitted and no endoscopic examination was made.

The case also impressed on us the fact that an endoscopic examination should be made, if possible, in all such acute conditions where a foreign body is suspected and the diagnosis is in doubt.

Dr. Manges' Discussion of Fig. 9.—It is perfectly evident from the film that there is displacement of the heart and upper mediastinal structures to the left, excepting that possibly the trachea is not displaced. I am not sure that one can see the shadow of the trachea in this case, but I just get the impression that it is not displaced to the left but perhaps slightly to the right. If I could be sure of this, then I would say that there was certainly some enlargement in the upper mediastinum that prevents displacement of the trachea to the left. And now, again, I am not able to say whether this film was exposed at inspiration or at expiration or whether it was of sufficient length to cover the entire breathing cycle. If so, then it seems to me that there is more evidence of collapse of the left lower lobe than there is of obstructive emphysema on the right side. The exposure is not as truly in the median line as it should be.

If you could assure me that this film was at the expiration, then I would say that there is absolutely no doubt about the presence of a rather marked obstructive emphysema of the right lung. At the fluoroscope, you would have seen this heart moving laterally and you would have been able to tell which direction it took during expiration. If it went to the left during expiration, then there is obstructive emphysema on the right side. If it went to the right during expiration, then there is evidence of atelectasis of the left lower lobe.

I agree that there is probably an enlargement of the thymus. It is entirely possible that the thymus is enlarged only on the left side.

You were certainly justified from the films in suspecting the presence of a nonopaque foreign body, but I cannot determine from them whether it was on the right or on the left side.

The following group represents a series of metallic foreign bodies in the bronchi and lungs.

CASE 11.—*No history, signs or symptoms.* M. C., a girl, aged 10½ years, had a common pin low down in the lung on the left side.

Because of suppurating cervical glands and keratitis, a roentgen-ray examination was made of the chest, which showed a common pin almost resting on the diaphragm on the left side. The patient was fairly well developed, she had no cough and her appetite and digestion were good. There were no physical signs. She has been under observation for over five years and the pin is still present in the same position.

The question of prognosis and surgical treatment comes up in the foregoing as well as the following case.

CASE 12.—Baby H., aged 16 months, had a common pin in the bronchus of the left inferior lobe.

The subjective symptoms and signs were more pronounced than in the foregoing case, but not severe. Attempts at endoscopic removal failed and she died following a thoracotomy. As we know that thoracotomy is a very dangerous operation in little children and such foreign bodies may remain in the lungs for many years without harm, it would seem best, except in rare instances, to be conservative and simply keep such patients under observation.

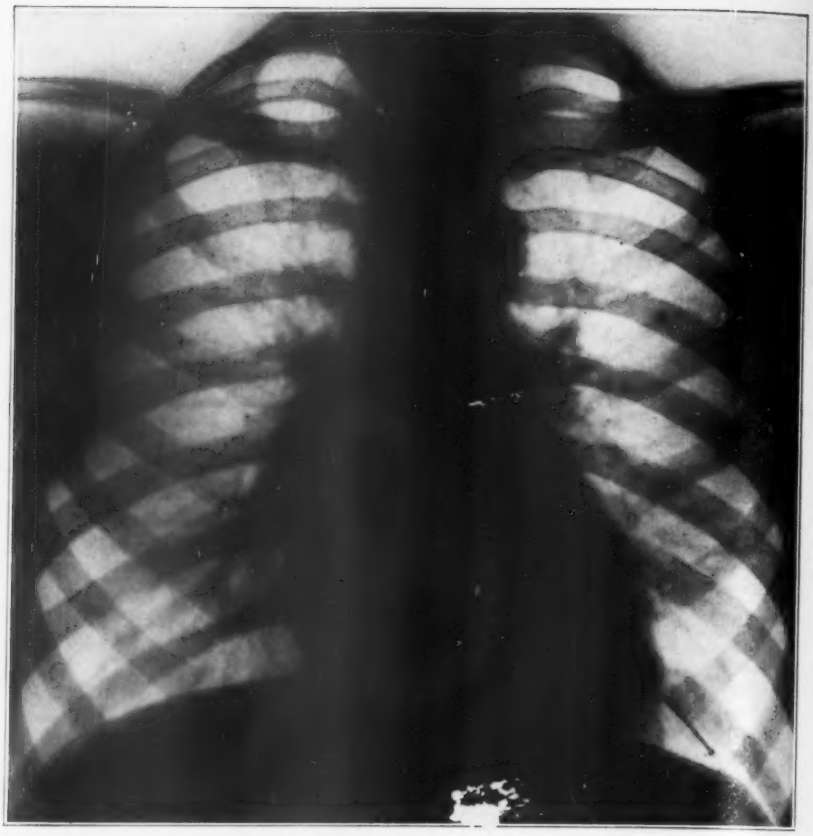

Fig. 10 (Case 11).—M. C., a girl, aged 10½ years, had a common pin low down in the lung on the left side.

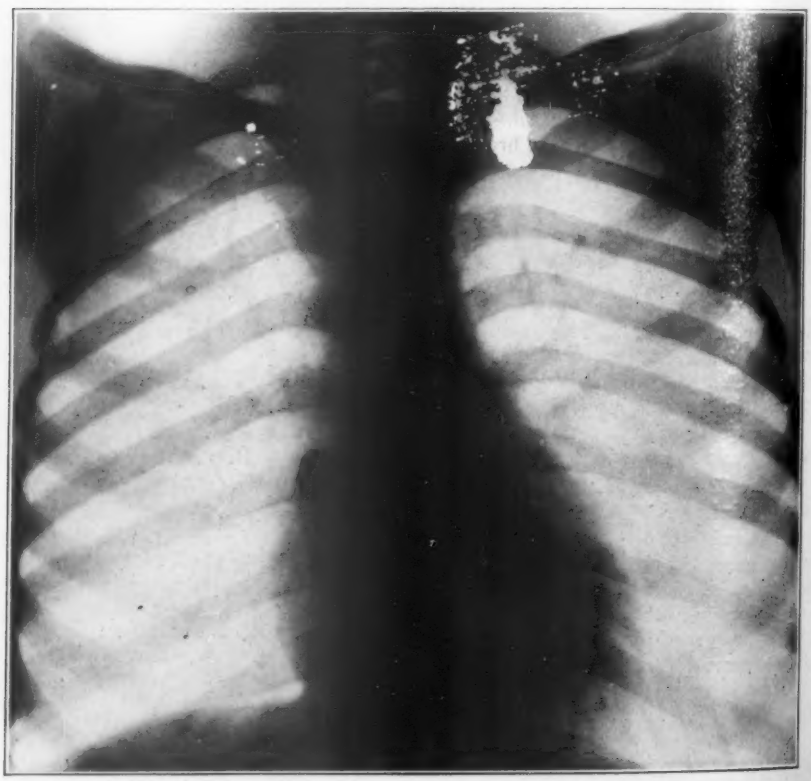

Fig. 11 (Case 13).—G. S., a boy, aged 9 years, had a pencil ferrule in the right lower bronchus with no history of aspiration.

CASE 13.—*A patient, without a history, treated for tuberculosis. The foreign body was discovered during the routine examination which included a roentgen-ray examination.* G. S., a boy, aged 9 years, had a pencil ferrule in the right lower bronchus. No history of aspiration of a foreign body could be obtained.

The patient was admitted to the Herman Kiefer Hospital with a diagnosis of tuberculosis. There was a history of fever, loss of appetite, slight cough and marked loss in weight, extending over a period of nine months. The physical examination showed decreased expansion on the right side with diminished resonance. There was dulness to the fourth rib in front, the eighth rib behind, fixation of the right half of the diaphragm, and faint breath sounds. The Pirquet test was negative. There was no sputum. The blood showed a total leukocyte count of 16,000, and differential count of polymorphonuclears, 65 per cent., small lymphocytes, 25 per cent., large mononuclears, 7 per cent., eosinophils, 3 per cent.

A routine roentgen-ray examination was made. The report stated that there was no evidence of tuberculosis or other pulmonary infection, but in the right lower bronchi there was a foreign body somewhat the shape of a tooth.

The foreign body was removed by peroral endoscopy. It proved to be a bent pencil ferrule minus the rubber.

In this case the long period without more definite symptoms was probably, in part, due to the foreign body being hollow and allowing the air to pass through it.

The important point to remember is that with localized lung symptoms which persist in spite of treatment with no positive signs of tuberculosis, but with an unexplained leukocytosis, gradual failure in health and weight, that a foreign body should be suspected.

If the foreign body in this case had been of the organic type, that is, nonradio-opaque, our roentgen-ray picture would have been of doubtful diagnostic value, the physical signs, however, were those of partial bronchial obstruction.

CASE 14.—*Acute case with complete obstruction of a main bronchus.* A. B., a boy, aged 4 years, had a brass screw in the left main bronchus causing complete obstruction.

There was sudden onset with high temperature, a persistent cough, marked dyspnea and cyanosis. The patient, a rapidly fatal case, was admitted to Harper Hospital with no history and a diagnosis of pneumonia.

The physical signs were decreased expansion with impaired resonance above and flatness below the fourth rib on the left. The breath sounds were intensely tubular above, below faint and distant, and over the flat area vocal fremitus was absent. The right side was hyperresonant with harsh breathing and numerous loud harsh râles.

The foregoing signs are those of complete bronchial obstruction and not of pneumonia. An obstructed bronchus in pneumonia is a rare condition, and when present should cause us to consider a foreign body as a possible etiologic factor.

The roentgen-ray picture (Fig. 12) on the obstructed side, is quite suggestive of that seen in atelectasis of the new-born. Complete obstruction is followed by collapse of the involved lung, a rapid development of secretions which cannot be expelled, and then we have the condition of "drowned lung." There is a compensatory emphysema on the uninvaded side, and as a result the mediastinal contents are pushed toward the side of the foreign body. The patient died on the fourth day. Such a condition is a surgical emergency.

CASE 15.—*Chronic case resulting in gangrene of the lung.* G. W., a boy, aged 5 years, had a shingle nail in right lower bronchus followed by gangrene of the lung.

The patient was admitted to Harper Hospital four months after the accident, with a diagnosis of empyema.

Following the roentgen-ray examination in the hospital, it was learned from the parents that they had repeatedly told their physicians of the boy's helping his father do some carpentry and choking on a nail. The roentgen-ray plate showed a nail in the right lower bronchus, and the irregular breaking down of the gangrenous lung.

The physical signs were decreased expansion, absent breath sounds, absent vocal fremitus, and resonance over the right lower lobe. These signs have frequently led to the diagnosis of empyema, abscess or bronchiectasis. The possibility of a foreign body should be considered in all such cases. A careful history and observation of symptoms would have made an earlier diagnosis possible.

Jackson [3] and others emphasize the following physical signs of foreign bodies in the bronchi. These signs vary in different cases and at different times in the same case. Secretions, normal and pathologic, may shift from one location to another; the foreign body may change position, admitting more, less or no air, or it may shift to a new location in the same lung, or even in the other lung. Small metallic bodies may produce no signs at all. The signs of diagnostic importance are chiefly those of partial or complete bronchial obstruction. The most characteristic physical signs are: (1) limited expansion; (2) decreased vocal fremitus; (3) impaired percussion note; (4) diminished intensity of breath sounds distal to the foreign body. Complete obstruction of a bronchus followed by "drowned lung" produces absence of vocal fremitus. Varying grades of tympany are obtained over areas of obstructive or compensatory emphysema. With complete obstruction there may be tympany from collapsed lung for a time. Râles in case of complete obstruction are usually most intense on the uninvaded side. In partial obstruction they are often found on the invaded side distal to the foreign body, especially posteriorly, and are often most intense at the site corresponding to that of the foreign body. A foreign body at the bifurcation of the trachea may give signs in both lungs.

ASPIRATION OF NURSERY POWDERS

In a recent popular article Jackson [2] mentions the foreign bodies commonly aspirated by children. He does not include the dangers of aspiration of substances such as baby powders, notably zinc stearate, a subject which is of especial importance, and has been frequently discussed in the literature of late. Heiman and Aschner [8] have reported a clinical study of twelve such cases, and the results of experiments with zinc stearate insufflation in animals. There is a usual history of the

8. Heiman, Henry, and Aschner, Paul W.: The Aspiration of Stearate of Zinc in Infancy, Am. J. Dis. Child. **23**:503 (June) 1922.

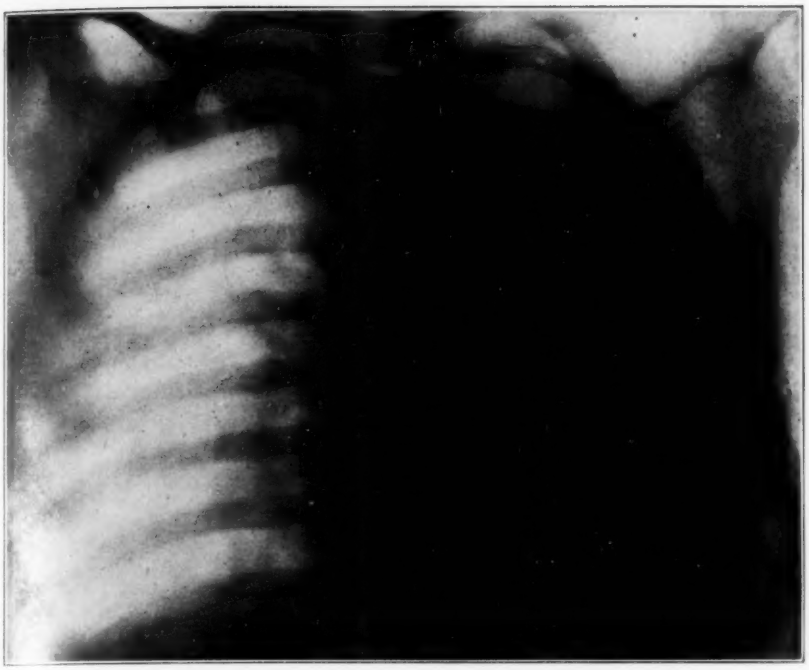

Fig. 12 (Case 14).—A boy, aged 4 years, had a brass screw in the left main bronchus causing complete obstruction.

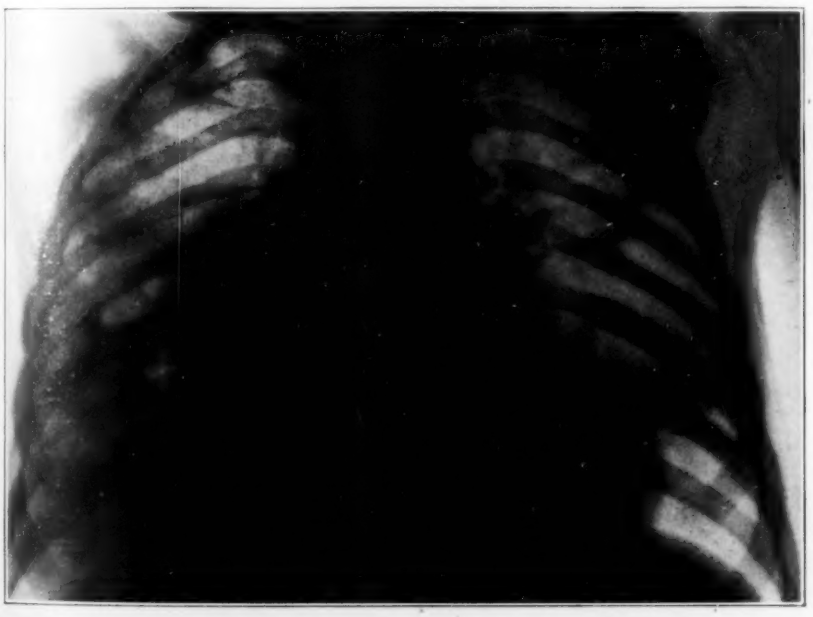

Fig. 13 (Case 15).—G. W., a boy, aged 5 years, had a shingle nail in the right lower bronchus followed by gangrene of the right lung.

infant playing with a powder box and spilling some of its contents on the face. The powder is thus aspirated into the bronchi and lungs. The onset of the trouble is sudden and stormy with rapid breathing and varying degrees of cyanosis. Complete asphyxia may occur and the condition rapidly becomes fatal. Few of the cases are of this fulminating type. A certain number develop signs of bronchopneumonia with symptoms of an acute toxemia which lasts from two to three weeks. The respirations are very rapid, the temperature is intermittent, varying from 99 to 105 degrees, and the pulse is small, weak and rapid. In a majority of their patients the severe initial symptoms subside during a period of three days. This is followed by a gradual recovery without signs of lung involvement. The diagnosis is evident from the history in these cases.

CONCLUSION

Foreign bodies in the air and food passages of infants and children are not of very rare occurrence. The initial symptoms are often not observed, and therefore no history is obtained, or the history may be obtained and not given sufficient consideration. Usually the higher the foreign body is lodged in the respiratory tract, the more pronounced the symptoms; while the lower down it is, the more marked the physical signs. Frequently in tracheal cases after the initial choking and strangling there is a symptomless period and then the tracheal symptoms develop. Esophageal foreign bodies of considerable size may produce no symptoms at first, but if allowed to remain in the esophagus for any length of time they may cause dangerous ulceration. The position of foreign bodies in the esophagus, as shown in the roentgen-ray plate, in relation to those in the trachea should be remembered.

Foreign bodies in the stomach rarely produce symptoms and no signs. With bronchial foreign bodies signs of partial or complete obstruction of a bronchus are diagnostically of the most importance. It is a characteristic sign to have a multiplicity and changeability of symptoms. Sometimes organic bodies may produce sudden violent attacks, at other times the physical signs and roentgen-ray findings may not develop until several weeks after the accident. Small metallic bodies frequently cause no reaction at all, while large metallic objects may produce symptoms simulating tuberculosis, or some other chronic lung infection. Aspiration of nursery powders may be extremely dangerous. Certain objects cannot be demonstrated by roentgen ray, while others make no shadow on the roentgen-ray plate, and still may give a diagnostic picture and definite signs and symptoms. Endoscopy should be resorted to in suspicious cases not demonstrable by roentgen ray. An early diagnosis may be of vital importance.

A fuller appreciation of these facts and of the importance of the history, signs and symptoms will help us to recognize more promptly

some of the unusual foreign body cases; it will assist us to differentiate the acute conditions from pneumonia, and the chronic cases from tuberculosis and empyema. It will remind us that the etiologic factor in bronchiectasis and gangrene of the lung may be a foreign body, and that a persistent wheeze is not always the result of anaphylactic or thymic asthma, but may sometimes be due to a foreign body.

2970 West Grand Boulevard.

TRANSPOSITION OF ABDOMINAL VISCERA. REVERSAL OF THE HEART CHAMBERS WITH LEFT-SIDED HEART*

EDWARD SHAW, M.D.,
AND
H. KINGSLEY BLAKE, M.D.
BOSTON

Dextrocardia and transposition of the viscera cannot be regarded as an extremely unusual anomaly, several hundred cases having been reported in the literature. The following unique case is reported because of the fact that, although there was transposition of the heart chambers, the heart occupied approximately its normal position and the clinical diagnosis was made on the abdominal findings.

REPORT OF CASE

H. B., a boy, aged 2 years, had been treated for phlyctenular conjunctivitis, and entered our wards with a complicating bronchopneumonia and otitis media.

History.—The family and past history were not obtained in detail. No information was elicited relevant to the present report.

Physical Examination.—The patient, a poorly developed and extremely malnourished boy, aged 2 years, was acutely ill. The left cornea was completely obliterated. The chest examination showed signs of pneumonic process near the angle of the right scapula. The heart was normally placed, the left border of dulness extended nearly to the nipple line, the right border by percussion, was in the midsternal line. There was no well defined apex impulse, but a systolic impulse was felt to the left of the lower end of the sternum and in the epigastrium. Sounds were best heard just to the left of the sternum at the fifth rib, and in the epigastrium, but were also well heard as far as the left nipple line and at the left border. A loud, rough, systolic murmur was heard all over the precordia but best in the locations where the heart sounds were loudest. No diastolic murmurs were heard.

Transposition of the abdominal viscera was suspected only when tympany was found over the area of normal liver dulness in the right midaxillary line. Gastric tympany was absent on the left, but analogous tympany was present in the right hypochondrium. Dulness was present over the lower thorax from the fifth rib downward to the costal margin. A sharp edge was felt on the left side 2 cm. below the costal margin, which could be followed a short distance toward the midline. At the right anterior axillary line an edge could be felt which could not be followed toward the midline.

Clinically it was thought that there was transposition of the abdominal viscera without demonstrable transposition of the heart. The systolic murmur was interpreted as probably functional in origin, although the possibility of its being a Roger murmur of patent interventricular septum was considered, particularly since with the transposed abdominal viscera other congenital anomalies of the heart would be suspected.

---

* Received for publication, May 28, 1924.

* From the Children's Medical Department, Massachusetts General Hospital.

Roentgen-ray examination confirmed the clinical findings regarding the position of the abdominal viscera, the liver was on the left and the "gas bubble" on the right. Fluoroscopy, after barium had been given, showed complete transposition of the stomach and intestines.

The heart shadows were unusual. Dr. George Holmes, of the roentgen-ray department, in interpreting the plate diagnosed a heart with transposed chambers, even though the greater part of the heart lay in the left chest. His interpretation stimulated further interest and resulted in electrocardiagraphic confirmation. In Figure 1 the cardiac outline can be seen. The smaller prominence above and to the right probably represents the aortic knob, that below being the left or systemic ventricle. On the left is the caval auricle. This is the mirror picture of a normally situated heart without the degree of displacement to the right which usually accompanies such transposition. Fluoroscopic study of the individual chambers was unsatisfactory because of the rapid heart rate and the child's condition.

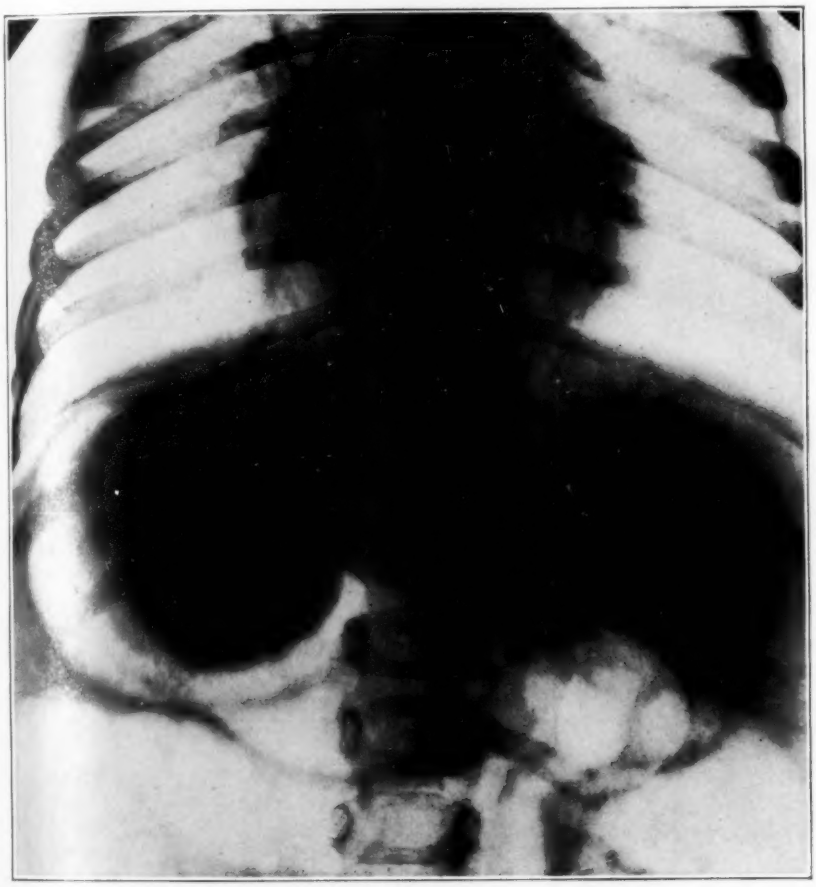

Fig. 1.—Chest plate, showing unusual form of the heart, with pneumonic process at the root of right lung.

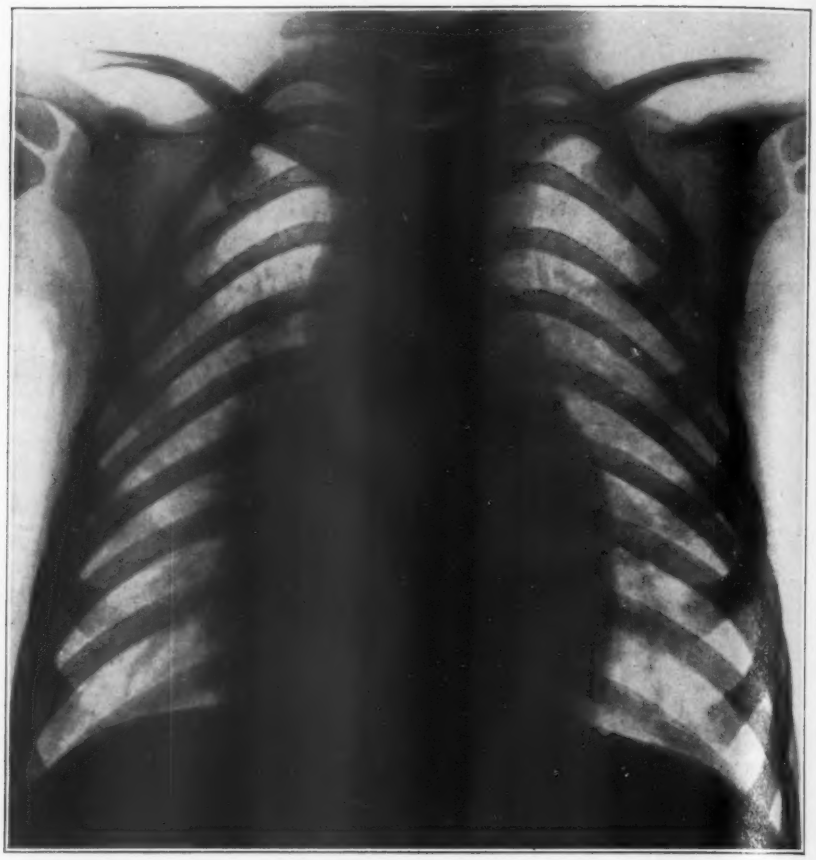

Fig. 2.—Transposition of abdominal viscera, following barium meal.

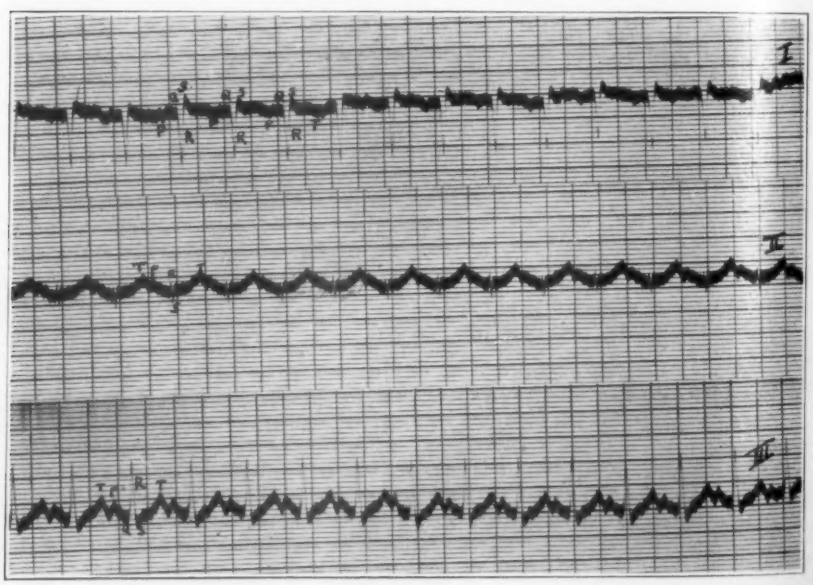

Fig. 3.—Electrocardiagram of dextrocardia: Lead 1, inversion of all complexes; right axis deviation; transposition of Leads 2 and 3.

In the right lung field was a fan-shaped shadow extending out from the right hilum, evidently pneumonia, explaining the temperature and respiratory symptoms.

Dr. P. D. White concurred in the diagnosis, and reported the electrocardiagram as showing "sino-auricular tachycardia, rate 140, dextrocardia—Lead 1 inverted with right axis deviation."

It has not been thought possible definitely to diagnose from the findings any cardiac anomaly other than transposition of the chmbers in a left-sided heart, although possibly other anomalies are present and may be indicated by the systolic murmur which has been interpreted as functional.

COMMENT

A case has been reported by Royer and Wilson,[1] which is somewhat similar. The abdominal viscera were completely transposed. The main portion of the heart was on the left of the midline, but the systemic ventricle was on the right. Their case, however, was practically a two chambered heart associated with extreme cyanosis. Abbott,[2] in her extremely complete review of dextrocardia, does not mention the occurrence of transposition of the chambers with left-sided heart.

Interest in this case centers chiefly in the occurrence of a transposition of the ventricles in a left-sided heart. It is of some practical importance that the occurrence of tympany in the right axilla over the area of normal liver dulness quickly led to the clinical diagnosis. Tympany in this location can mean only transposed liver or the presence of gas between liver and diaphragm. The latter is readily ruled out and the association of dulness in the left axilla quickly led to the correct diagnosis.

---

1. Royer, B. F., and Wilson, J. D.: Incomplete Heterotaxy, Arch. Pediat. **25**:881 (Dec.) 1908.

2. Abbott, Maud: Modern Medicine, Osler and MacCrea, Philadelphia, Lea and Febiger, 1915.

BRAIN ABSCESS

REPORT OF AN UNUSUAL CASE *

M. G. PETERMAN, M.D.
ROCHESTER, MINN.

This case is reported to illustrate the difficulty encountered in the diagnosis of intracranial lesions. There was so little to suggest an abscess that the possibility of it was not considered in reaching a diagnosis.

REPORT OF CASE

The patient was a boy, aged 11 years, whose family history was free from hereditary diseases. He had been treated at the Mayo Clinic in May, 1917, for phlyctenular keratitis. There was also a history of mumps, chickenpox, and two attacks of measles. He had had no illnesses, accidents, or injuries during the last five years, and very careful questioning failed to reveal a history of a "cold," "running nose" or "sore throat" during the three months before the onset of the present illness.

Jan. 22, 1924, the patient complained of bilateral, frontal headache, to which he had not previously been subject. At first the headaches occurred only on arising in the morning and were alleviated by reclining. After the first week the headaches increased in severity and the patient vomited from two to five times daily. The vomiting was not projectile. During February, there were several intervals of from two to four days when the boy was free from headache, nausea and vomiting, and he retained his food. He attended school until January 31, then remained at home for the next two weeks, but was not put to bed until February 15. At about this time he complained of dizziness several times. February 27 he had visual illusions, delusions, and hallucinations, and "talked peculiarly" several times. The family physician noted that the patient's pulse rate was slow (50), and called for a consultation.

On examination of the child in the home he was dull, in no apparent pain, and had a clear sensorium. Several times during the examination he plucked at the bed clothes, and picked his nose. His skin was sallow. There was a suggestive Macewen's sign over the anterior part of the skull. The pupils were equal, regular, and reacted to light and in accommodation. The nose, throat and ears appeared normal. There was one carious tooth. The findings in the chest were negative. The abdomen was scaphoid and slightly tender on deep pressure. The extremities showed nothing abnormal. The Brudzinski and Kernig signs were suggestive, and the Zinda sign was positive. The patellar reflexes and the superficial abdominal reflexes were not obtainable; all other reflexes were normal. The mouth temperature was 99, the pulse rate was 52, and the respiration 18. The leukocytes numbered 13,750, of which 87 per cent. were neutrophils; 10.5 per cent. lymphocytes; 1.5 per cent. transitionals, and 1 per cent. large mononuclears. Examination of the urine was negative.

A clear fluid under moderate pressure was obtained by spinal puncture. The fluid showed a positive Nonne reaction with a cell count of 43 lymphocytes, and 16 polymorphonuclears for each cubic millimeter. Smears and culture of the fluid did not reveal organisms. A diagnosis was made of increased intracranial pressure secondary to tuberculous meningitis or brain tumor. February 28, the right pupil was larger than the left. February 29, the Pirquet reaction

* Received for publication, May 27, 1924.
* From the Pediatric Section, Mayo Clinic.

was positive (4 mm.). Both pupils were dilated and equal. The spinal fluid was under a moderately increased pressure, and contained 26 small lymphocytes for each cubic millimeter. The Wassermann test on the spinal fluid was negative. No organisms were found on smear or culture. March 1, the right palpebral fissure, and the right pupil were larger than the left. The fields were roughly normal. The fundi showed bilateral choked discs of from 2 to 3 diopters, with rather acute hemorrhages and exudate. March 2, a slight convulsive seizure was reported.

March 3, the patient was brought into the hospital. Examination on admission showed that he was lethargic and ataxic without additional motor or sensory impairment. There was slight mental confusion. The eyes showed little change from the examination of March 1. The Brudzinski, Kernig, and Zinda signs were all definitely positive. The spinal fluid was under a slight increase in pressure, and contained 23 small lymphocytes and 24 polymorphonuclear leukocytes for each cubic millimeter. There were no organisms found on smear or

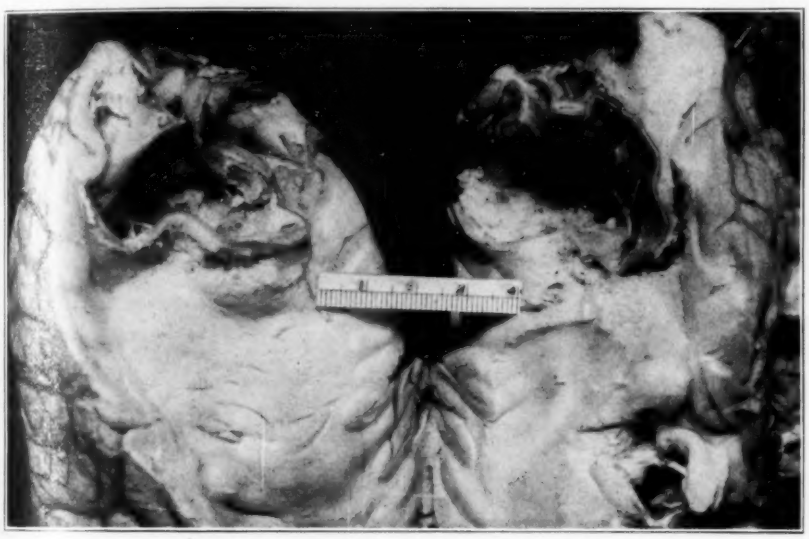

Fig. 1.—Abscess in the left frontal lobe.

culture. Roentgenograms of the skull disclosed the marked increase of intracranial pressure. The patient's condition grew progressively worse, and he died of respiratory failure March 6.

Necropsy.—The cranial vault was thin, and there were small localized areas of rarified bone. The dura was markedly thickened and adherent to the cranial vault. The right cerebral hemisphere was noticeably congested, but showed no other gross lesion. The convolutions of the left frontal area were flattened. The left frontal lobe was bulging, and was of a greenish-yellow color, soft, cystic and fluctuating. On section, an abscess was found which measured 5 by 4 cm., from which about 60 c.c. of greenish-yellow exudate escaped. At the base of this abscess there was a small continuous cavity, probably a recent extension of the primary abscess toward the base of the brain. The pia covering this area was cloudy and showed in a small area a definite purulent exudate. The lateral ventricles were dilated 2 (on the scale of 1 to 4), and contained slightly cloudy, yellowish fluid. The third and fourth ventricles were not dilated. The blood sinuses showed no antemortem thrombi. The accessory sinuses and mastoid cells were normal. On microscopic section of the brain,

numerous small petechial hemorrhages were seen throughout the cortex. The abscess is shown in Figure 1. The thick wall of the abscess, consisting of considerable connective tissue, is shown in Figure 2. Culture of the abscess in the left frontal lobe revealed staphylococcus in pure culture. Cultures of the blood and spleen were negative.

COMMENT

Microscopic section of the abscess demonstrated that it must have existed for some time before the onset of symptoms. It has been estimated that from two to three weeks are required for the formation of a capsule around a brain abscess. This patient's symptoms probably began when a second, smaller abscess formed, by extension, from the initial lesion, and reached the surface.

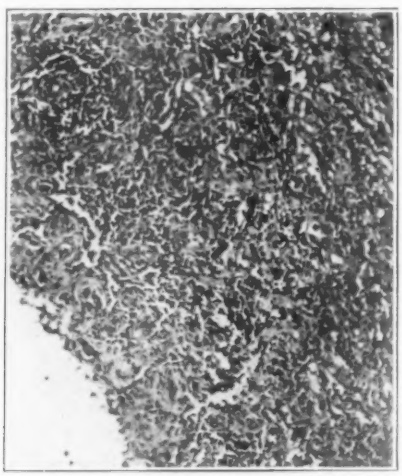

Fig. 2.—Low-power photomicrograph of wall of abscess; × 60.

The differential diagnosis in this case included tuberculous meningitis, brain tumor and brain abscess. One of the most important points in the differentiation of these three conditions is the history. Brain abscess was not considered because there was no history of a previous infection of the skin, nose, throat, ears, or gastro-intestinal canal; there were no localizing symptoms, the lesion being located in the "silent area"; the increased cell count of the spinal fluid consisted mainly of lymphocytes. Brain abscess is almost always secondary to an infection elsewhere in the body, usually otitis media, accessory sinusitis, compound fractures of the skull, pyemia, bacteremia, abscess of the lung and other infections. The cells found early in the spinal fluid of patients with brain abscess are usually polymorphonuclear leukocytes. Cerebral abscess is rare in children, and is hardly to be considered without a history of a previous infection. Brain tumor in children, producing signs of increased intracranial pressure, with a choked disc of from 2 to 3

diopters, with no localizing symptoms, and no disturbance of respiration, with a spinal fluid cell count, consisting mainly of lymphocytes, of fifty-nine cells for each cubic millimeter, is quite uncommon.[1]

The positive tuberculin reaction, the history of phlyctenular conjunctivitis, the insidious onset, without antecedent acute infection, all point to a tuberculous involvement of the meninges, or to a possible tuberculoma. Clinically, a new growth could not be excluded. It was, therefore, rather a surprise at necropsy to find that the symptoms had been due to a staphylococcal abscess and not to a tuberculoma or cerebral neoplasm.

---

1. Tuberculous meningitis and brain abscess often present very similar syndromes. The onset in either may be insidious or acute; the temperature is low, and the pulse slow. The spinal fluid may be under increased pressure, clear and with a moderate increase in the cell count. In the early stages of brain abscess, the cells are usually polymorphonuclear leukocytes, whereas in tuberculous meningitis they are generally lymphocytes.

ICTERUS GRAVIS OF THE NEW-BORN*

PAUL KLEMPERER, M.D.

NEW YORK

Jaundice occurs in the new-born baby so frequently that its appearance is considered a mere physiologic event, and owing to its usually mild and transient course it has caused no serious concern to the pediatrician. It is obvious that, owing to its frequency in the postnatal period, jaundice will usually be an accompanying symptom of pathologic conditions in the new-born baby. In these cases our diagnostic and therapeutic efforts will concentrate on the chief disease, and the jaundice does not warrant any other consideration than the mere physiologic icterus of the new-born. Cases, however, in which the jaundice is the outstanding symptom of a severe illness deserve serious consideration. The underlying pathologic changes in one group of cases of this general type will be clearly indicated by the acholic feces as an obstruction of the outflow of the bile, due to malformation of the large bile ducts. In another group, the icterus can be recognized as an accompanying symptom of a septicemia and is better designated as septic jaundice. As icterus gravis, however, in a clinical sense, we would designate cases of severe jaundice, usually with fatal outcome, which do not fall in either of the foregoing groups. The underlying pathologic changes in these cases can only be revealed by an exact bacteriologic examination and a thorough anatomical and histologic analysis. Three cases of this type, which have recently come within observation, form the subject of this paper. Unfortunately, a bacteriologic examination was omitted in one of these cases. The histologic findings, however, proved to be of such interest that we felt justified in including this case in our report.

REPORT OF CASES

CASE 1.—The first patient, a well developed boy who weighed 11½ pounds (5 kg.) at birth, was admitted to the New York Post-Graduate Hospital with severe jaundice, which had started on the second day after birth. During his stay in the hospital he developed a hemorrhagic condition, hemorrhages under the skin from the cord and anus. Although transfusion had been performed, the patient died fourteen days after birth. A bacteriologic blood examination the day before death revealed a small gram-negative bacillus which was not definitely identified and was questioned as a contamination. The Wassermann test was negative. The necropsy was performed twenty-three hours after death by Dr. W. J. MacNeal, to whom I am indebted for the report of the case. There

* Received for publication, May 26, 1924.

* From the Department of Pathology and Bacteriology, New York Post-Graduate Medical School and Hospital.

* Read before the convention of American Pathologists and Bacteriologists, Buffalo, April 19, 1924.

was marked jaundice and numerous subcutaneous and subperitoneal blood extravasations. The umbilical cord was not sloughed off yet but did not show suppuration. The liver was large, green and unusually soft. The bile ducts were patent. The gallbladder was very moderately distended. The kidneys showed marked icterus of the cortex. The histologic examination of the liver, unfortunately, showed advanced necropsy changes. Nevertheless, it was possible to discern certain features which might throw some light on this case. The lobular markings could not be distinguished. The liver cells did not form coherent columns, but lay very loosely between the meshes of a very wide net-

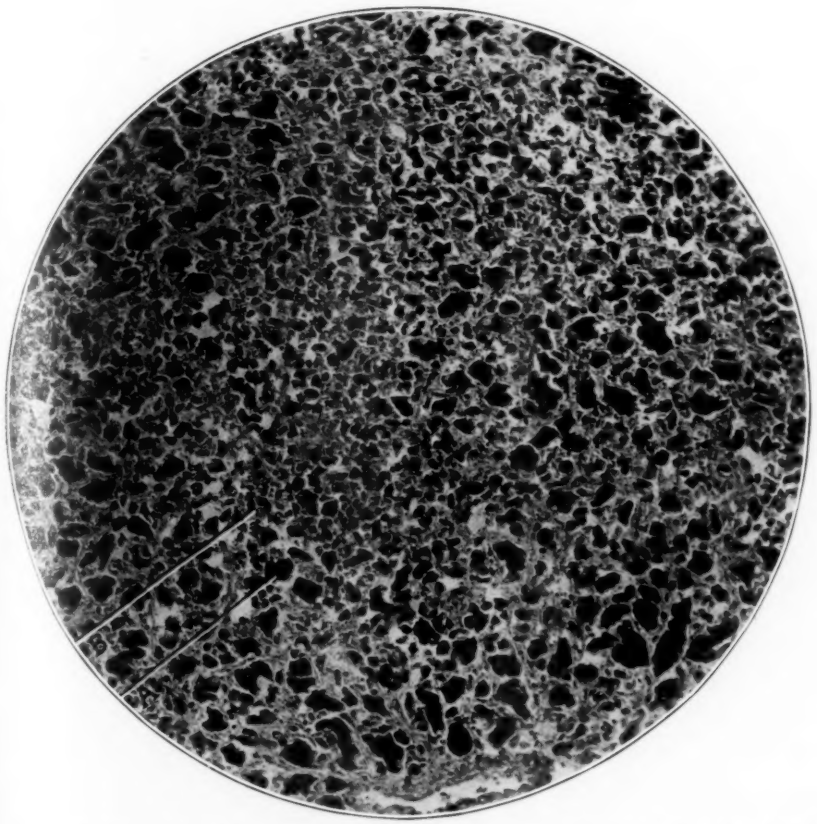

Fig. 1 (Case 1).—Liver lobule showing the irregular liver cells. (*a*) Large cells at the periphery. (*b*) Small disintegrated cell in the center.

work of fibers which stood out conspicuously. They varied widely in shape and size. There were cells the size of a normal liver cell, polyhedral in shape, with a round vesicular nucleus and with one nucleolus, occasionally grouped in short columns, and small isolated cells of irregular shape with very faintly stained nucleus. Among these there were quite irregular structures without nuclei, for the most part densely filled with greenish-brown droplets and casts, apparently bile pigment. Frequently, one could find meshes which were practically empty or contained cell débris and several polymorphonuclear leukocytes and lymphocytes. All the cells contained droplets and sausage shaped casts of bile

and occasional fat droplets. The liver cells were best preserved in the parts around the periportal fields, but even here the cells formed only short bands and there was cell débris between the well outlined liver cells. The capillaries were wide and frequently filled with lymphocytes and polymorphonuclear leukocytes. The latter occasionally contained small brown granules. The periportal fields were narrow, and did not show cell infiltration or bile duct proliferation. Examination of the large bile ducts showed an open lumen; the epithelial lining was exfoliated and lay in the lumen. The wall did not show any changes. The lumen of the umbilical vein was open but narrow; there were no changes to be seen in the wall. The spleen showed marked hemosiderosis. Stain with

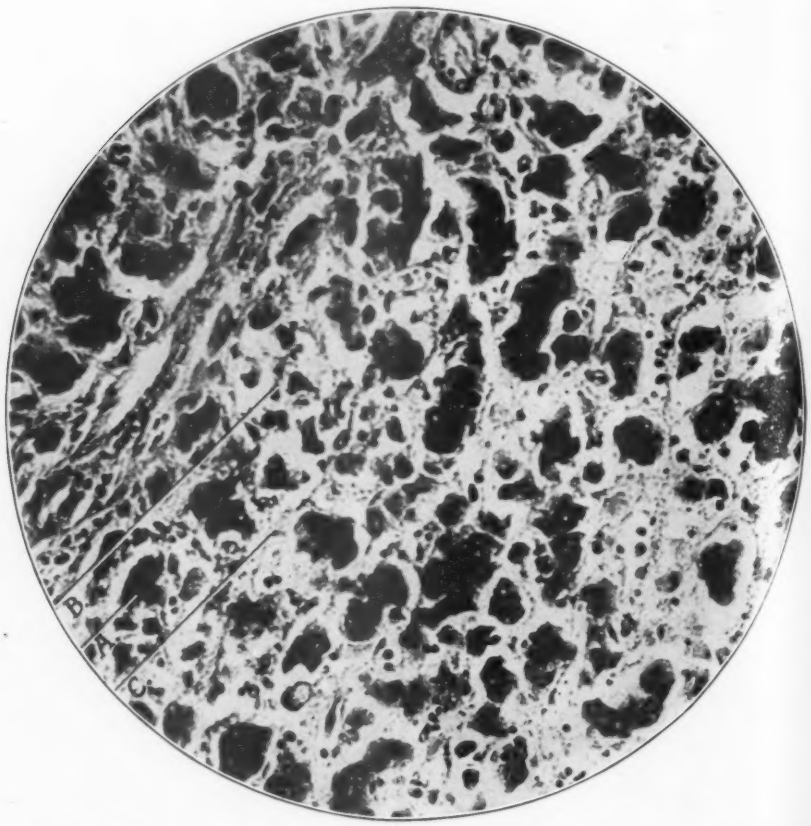

Fig. 2 (Case 1).—High magnification. (*a*) Large liver cell. (*b*) Small necrotic cell. (*c*) Cell débris.

sudan III did not show fatty changes in the heart muscle and kidneys. The kidneys showed bile casts in the cortical tubules; their epithelial lining showed impregnation with bile but was well preserved. Glomeruli were negative. Stains for spirochetes and bacteria in the liver were negative.

CASE 2.—The second patient, a well developed boy, who weighed 12 pounds (5.4 kg.) at birth, was admitted to the Hospital with jaundice, which had begun the third day after birth. During his stay in the hospital he developed a severe attack of jaundice. There were no external hemorhages but the feces showed strong blood reaction. The temperature was around 99 until the last days

when it rose to 104 and 105. Although transfusion was performed, the patient died 21 days after birth. The blood Wassermann was negative. Necropsy was performed the same day by Dr. MacNeal, who turned the case over to me. There was generalized jaundice; the umbilicus was healed. The liver was large, and weighed 270 gm., was firm in consistency, externally brownish-gray and on section distinctly yellowish. The gallbladder was very moderately distended and bile readily expressed through the papilla of Vater.

Histologic Examination.—The lobular structure of the liver stood out very clearly, even more so than in the normal organ. That was accomplished by the fact that the periphery of the lobules was formed by large liver cells with abundant cytoplasm, which contrasted with the midzonal and central portions.

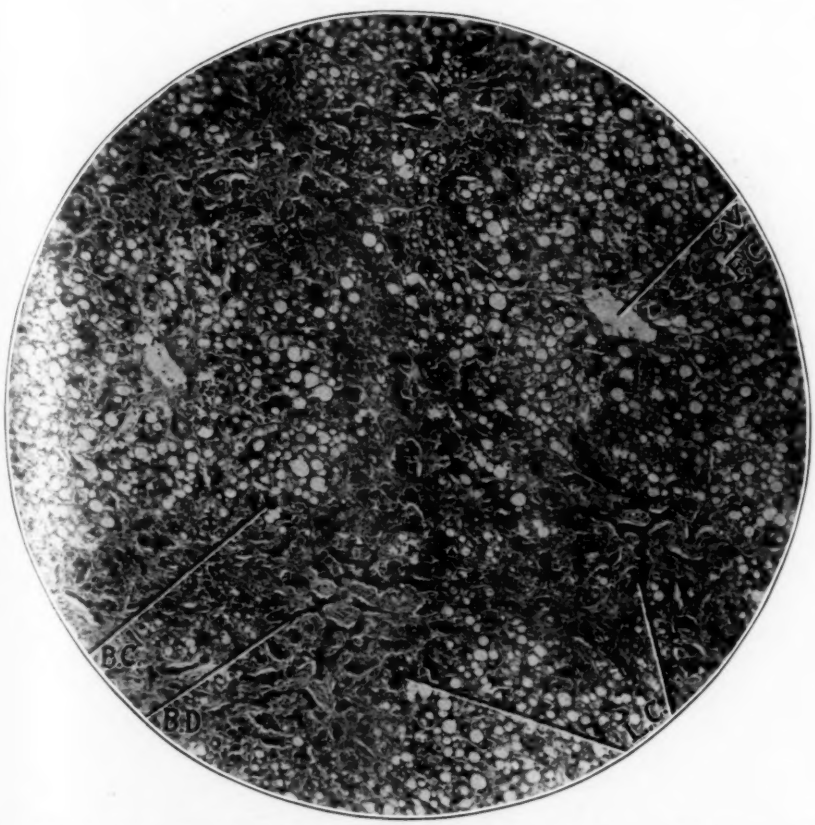

Fig. 3 (Case 2).—Two liver lobules. (*cv*) Central vein. (*fc*) Liver cell containing fat. (*lc*) Large liver cells at the periphery. (*bd*) Proliferated bile ducts. (*bc*) Bile casts.

Here the cells were completely filled with large fat droplets, which pushed the nucleus to the periphery of the cell. Among these cells, which did not show an arrangement in columns, occasional small cells with deeply-stained nuclei and brownish-green pigment or without nucleus were found. The periportal fields were conspicuously wide and showed numerous tubular structures which extended toward the center of the lobules, proliferated bile ducts. Frequently casts and droplets of green bile could be seen between the cells.

The large bile ducts and the umbilical vein did not show any changes. The heart muscle and kidneys did not show fatty changes or parenchymatous degeneration. The spleen showed marked hemosiderosis. The lower lobes of the lungs showed foci of bronchopneumonia.

CASE 3.—The third patient, a boy, was well developed but very feeble; his birthweight was 5 pounds (2.3 kg.). He was admitted to the Babies' Ward November 16, aged 15 days. He had been jaundiced for more than eight days. He did not take food. The patient was deeply jaundiced, was in a very serious condition and died the next day. The Wassermann test was negative.

Necropsy was performed twenty-five minutes after death. The skin and

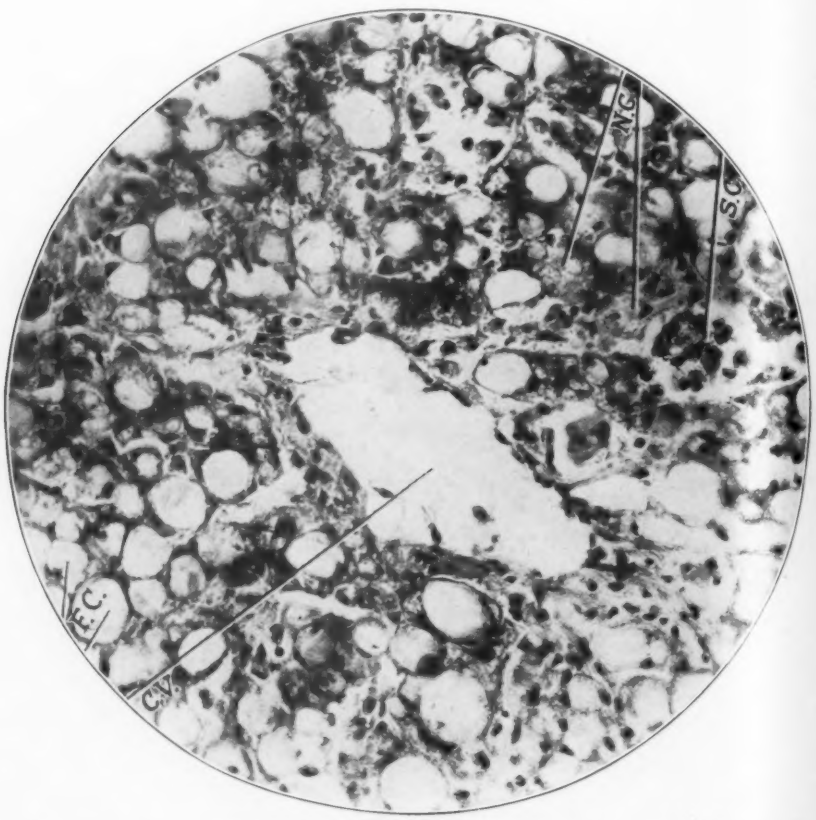

Fig. 4 (Case 2).—High magnification. (*cv*) Central vein. (*fc*) Liver cell containing fat. (*sc*) Small liver cells without fat. (*nc*) Necrotic cells.

sclera were markedly yellow. The umbilicus was healed. There were small petechiae of both pleurae. The liver measured 80 by 60 by 28 mm.; Glisson's capsule was smooth; on cross section it was yellow, and the lobular structure was indefinite. The gallbladder was filled with green bile, and bile was readily expressed through the papilla of Vater. The left and right hepatic ducts were patent. Near the common duct there was a yellow lymph node, 3 mm. in diameter. The medulla of both kidneys showed a deep yellow-orange tint. Bacteriologic examination of the heart, blood, lungs and spleen revealed a few colonies of a hemolytic strain of *B. coli*.

Microscopic Examination.—The structure of the liver lobules was intact. The periportal fields were narrow and did not show cellular infiltration. The liver cells were arranged in almost straight cords directed toward a central vein. They frequently contained a yellow pigment in finer or coarser granules. The finer granules gave an iron reaction; the coarser ones did not. By treatment with potassium hydroxid and nitric acid a few granules turned blue. Sudan stain revealed small fat droplets in the cells, without preference for the peripheral or central parts. Glycogen was present in the cells, even in those which contained bile pigment. The most conspicuous feature was the great number of large mononuclear cells in the sinusoids of the liver. The nucleus of these

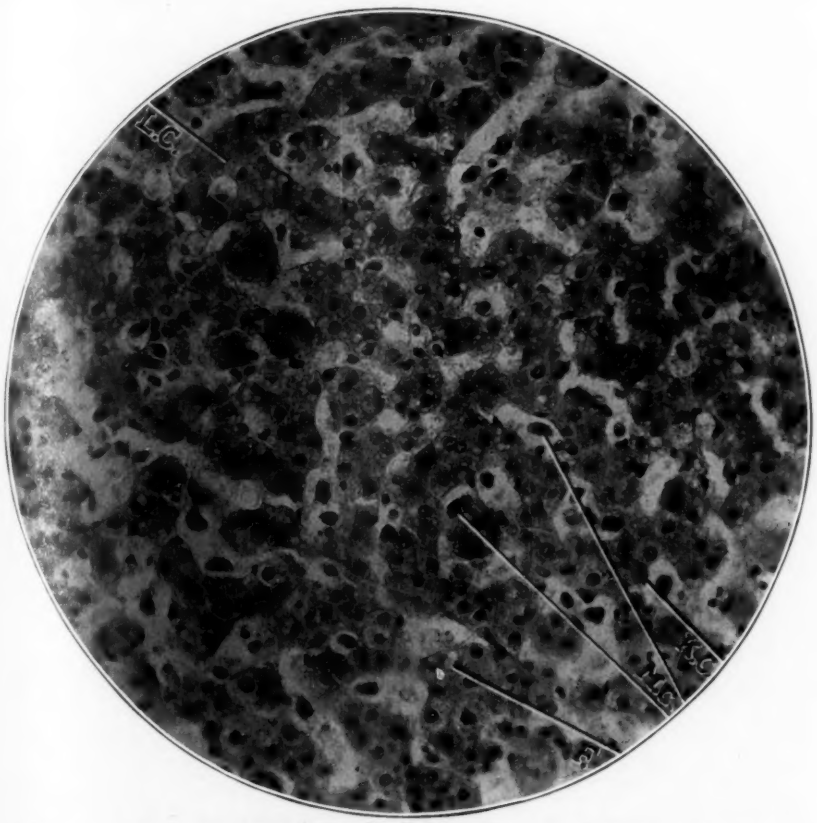

Fig. 5 (Case 3).—(*lc*) Regular liver-cell cord. (*f*) Fat droplet in liver cell. (*mc*) Large mononuclear cells in capillaries. (*kc*) Kupffer cell.

cells was rather poor in chromatin, oval and frequently kidney-shaped. The cytoplasm was densely filled with small brown pigment granules which gave intense iron reaction, but frequently the cytoplasm stained diffusely blue with ferrocyanate-hydrochloric acid. Besides that pigment, which on account of its reaction must be considered as hemosiderin, we occasionally found yellow pigment granules included in these cells which did not give the Prussian blue reaction. They coincided in their morphology and in their negative iron reaction with the yellow pigment found in the liver cells. Frequently, the cytoplasm

showed vacuoles the size of a red blood cell and smaller. In sections stained with sudan III these vacuoles remained unstained.

The spleen showed very small malpighian bodies choked by a proliferation of the large mononuclear cells of the pulp, which stood out conspicuously. The sinusoids of the spleen were dilated, densely filled with blood and contained numerous large mononuclear cells. With higher magnification the mononuclear cells were recognized as containing very frequent large and small vacuoles, sometimes several in one cell. Iron pigment granules were found in them and generally the cytoplasm stained diffusely blue with ferrocyanate. Special stain

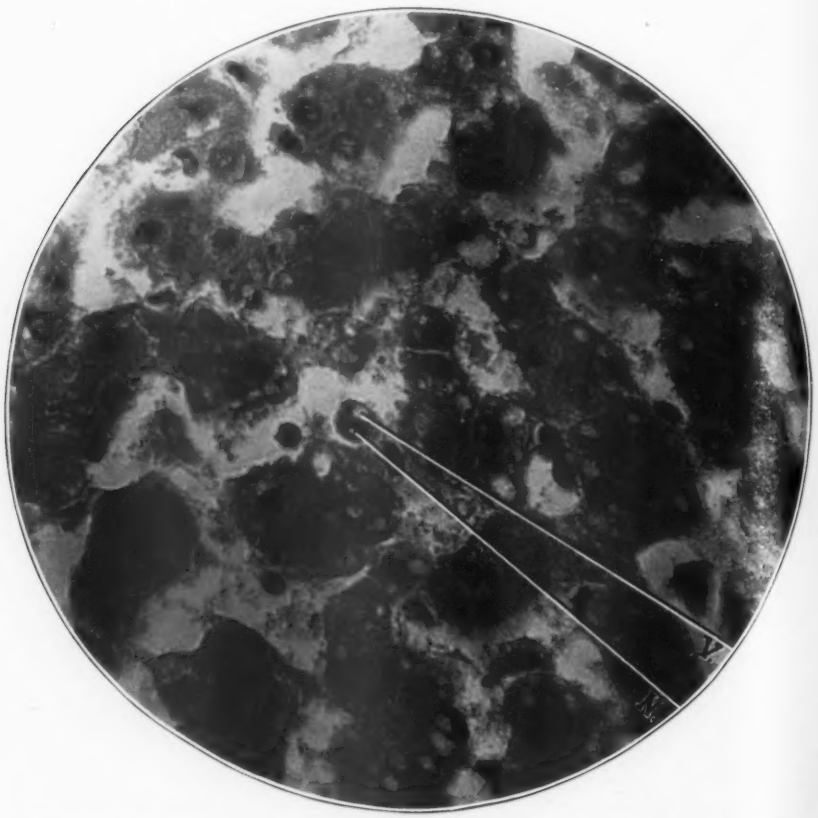

Fig. 6 (Case 3).—High magnification. Large mononuclear cell. (*n*) Nucleus. (*v*) Vacuole.

for hemoglobin, devised by Lepehne, showed that the vacuoles contained small sharply outlined hemoglobin droplets and that very numerous mononuclear cells contained phagocyted erythrocytes. This concerned both the cells in the pulp as well as the large cells in the sinuses. The cells found in the sinuses of the spleen were identical in their structure with those present in the liver sinuses.

The heart muscle was unchanged. The lungs showed bronchopneumonia, and in the foci a large number of small bacilli were found. The tubules of the medulla of the kidney contained crystals of bilirubin.

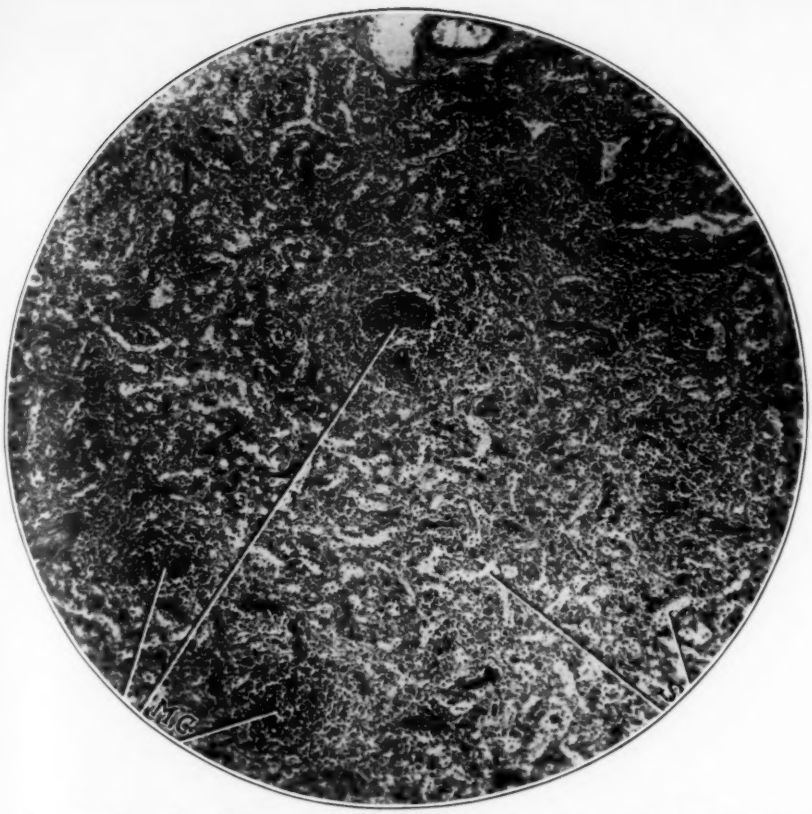

Fig. 7 (Case 3).—Spleen. (*Mc*) Malpighian corpuscle. (*s*) Venous sinus.

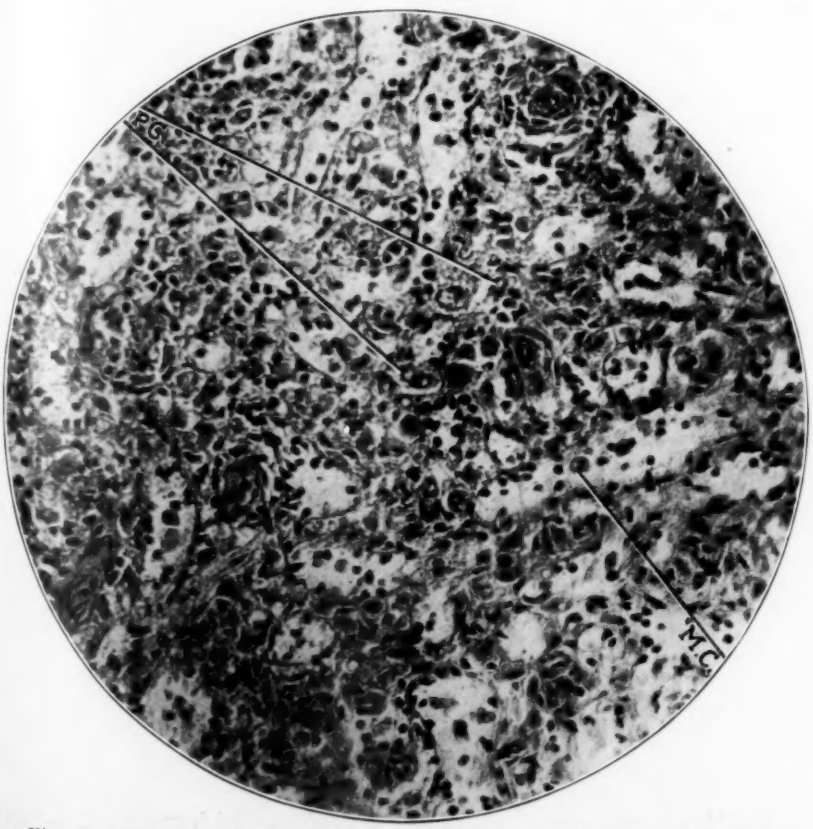

Fig. 8 (Case 3).—Spleen, high magnification. (*pc*) Pulp cells showing vacuoles in their cytoplasm. (*mc*) A large mononuclear cell with vacuolized cytoplasm in a venous sinus.

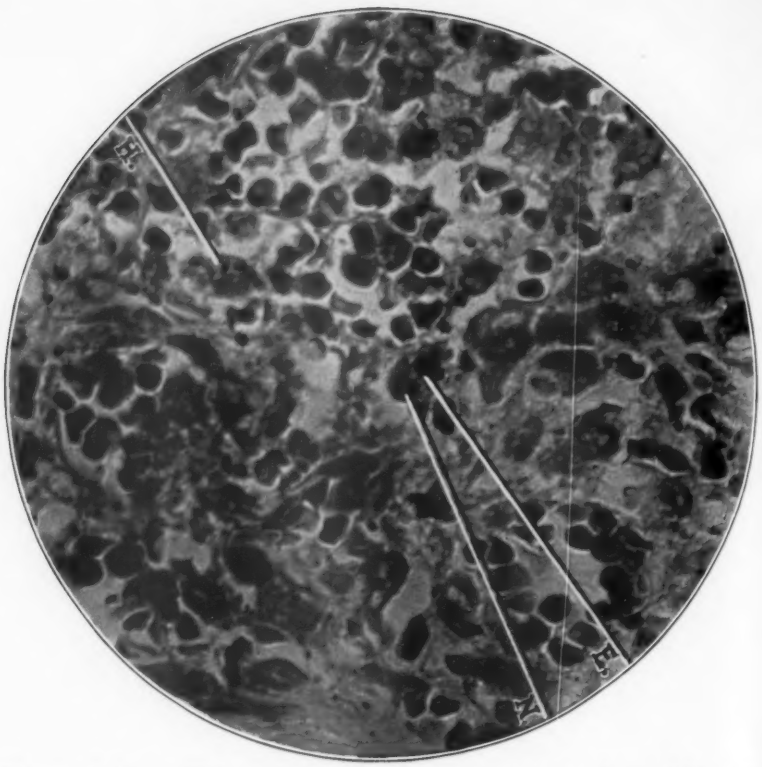

Fig. 9.—Spleen. High magnification. Lepehne stain for hemoglobin. Pulp cells. (*n*) Nucleus. (*e*) Phagocyted erythrocyte. (*h*) Hemoglobin droplet in a vacuole.

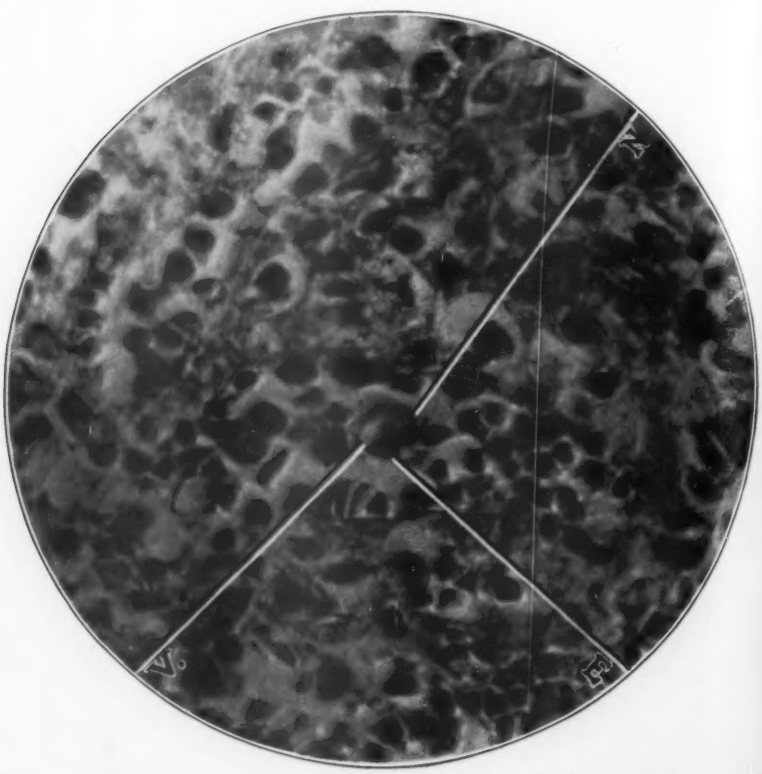

Fig. 10.—A mononuclear cell in a venous sinus. High magnification. (*n*) Nucleus. (*e*) Phagocyted erythrocyte. (*v*) Vacuole in cytoplasm.

COMMENT

The histologic examination of the first two cases revealed severe changes of the liver. They consisted in the first case of a diffuse, not focal necrosis and destruction of the liver cells, which was most conspicuous but not limited to the central areas of the lobules, and had led to an alteration of the lobular architecture of the organ. Fatty changes were present but only to a moderate extent. We may infer from the histologic picture that the destructive process had been of some duration because we found occasionally absence of liver cells in small foci, infiltrating wandering cells removing the cellular débris and advanced recovery of the liver cells, particularly near the periportal fields.

Extensive necrosis of liver cells, with less conspicuous degenerative fatty changes, are the characteristic histologic features of acute yellow atrophy. The reparation and regeneration of the destroyed liver tissue in acute yellow atrophy originates in the surviving and less altered peripheral liver cells and eventually sprouts from proliferating bile ducts. We could see in our case that there had been an advanced reparation of large liver cells near the periportal fields but no bile duct proliferation. The extensive necrosis without marked fatty changes, and the partial reparation in the periphery of the lobules, certainly coincide with the picture of acute yellow atrophy in a later stage. The gross picture of the large liver, however, does not fit the picture of acute yellow atrophy. Acute yellow atrophy in childhood is not a common occurrence and it is certainly very rare in the new-born. I was able to find only four cases recorded in the literature, those of Hecker,[1] Pollitzer,[2] Aufrecht,[3] and Stransky.[4] The cases recorded by Graham [5] cannot be considered as acute yellow atrophy because there was no necrosis. French authors, however, Durante [6] and his associates, have reported that liver changes identical to acute yellow atrophy may occur as sequelae of umbilical septicemia. It must be asked whether our case does not belong in this group. There was clinical evidence of navel infection, and the necropsy protocol records an extensive blood extravasation in the umbilical region. The bacteriologic examination of the blood revealed a microorganism which, however, was not definitely established as a pathogenic agent. The hemorrhagic condition of the baby cannot be considered as definite evidence of septicemia, because it might have been the result of the cholemia present. Although there

1. Hecker, C.: Monatschr. f. Geb. u. Frauenkrankh. **29**:321, 1867.
2. Pollitzer: Jahrb. f. Kinderh. **3**:40, 1860.
3. Aufrecht: Zentralbl. f. inn. Med. **17**:273, 1896.
4. Stransky, E.: Monatschr. f. Kinderh. **23**:500 (Aug.) 1922.
5. Graham: J. Exper. Med. **15**:307, 1912.
6. Durante: Bull. soc. d'obst. et de gynéc. de Par. **10**:303, 1907.

are certainly many arguments in favor of the diagnosis of septicemia, it must be emphasized that the anatomic and histologic examinations did not furnish confirmatory evidence. Search for bacteria in the liver and the spleen was negative. The histologic picture of the spleen, which was rather large on gross examination, was not suggestive at all of septicemia. There were no fatty changes found in heart muscle and kidneys, and, above all, the umbilical vein did not show suppuration. Therefore, the question as to whether the liver changes have to be considered as the result of a septicemia cannot be decided. Here the same problem is faced which is met with in cases of acute yellow atrophy in adults. The occurrence of small foci of necrosis in the liver is quite a common picture in septicemia, but extensive, diffuse necrosis with preference to the central portions of the lobules is extremely unusual, although acute yellow atrophy might be the result of bacterial infection. The same consideration holds for the cases of septicemia in children. However, the case may be, it may be said that the icterus in Case 1 was due to a destructive process in the liver related to the pathologic condition of acute yellow atrophy.

The outstanding features of the liver alteration in the second case are the extensive fatty changes in the intermediary and central zone of the lobules, and the conspicuous bile duct proliferation and reparation of liver cells in the periphery. The fatty changes can be considered to be of a degenerative, not merely infiltrative type, because occasional necrosis among the cells were found. Extensive fatty changes of the liver in icteric conditions of the new-born have been described in the acute fatty degeneration of the new-born, the so-called Buhl's disease, and in Graham's experiments on the pathologic changes of hemorrhagic disease. Buhl, as well as Graham, emphasizes the analogy in the liver changes in their cases with those found in acute phosphorus poisoning. The similarity of the foregoing case to the phosphorus liver is very striking, which represents a subacute stage of the disease of the new-born. It follows, even in the latter stage, the example of the liver changes in prolonged phosphorus poisoning by the regeneration and bile-duct proliferation in the periphery of the lobules, and the sporadic necrosis of the liver cells, besides extensive fatty changes. Thus the case before mentioned adds further evidence in the formal genesis of icterohemorrhagic condition of the new-born. With regard to etiology, however, we are unable to add any positive information. Buhl's disease has been agreed on by the majority of recent writers to be neither a clinical nor a pathologic entity but merely a condition of septicemia in the new-born. Graham, however, subsumes Buhl's disease together with the hemorrhagic disease as a pathologic condition, brought about by a multitude of causes which have one common under-

lying principle: the lack of oxygen. In human beings, Graham maintains that it is principally due to asphyxia or chloroform applied during labor.

These causes cannot account for the foregoing case, since especial inquiry made on both points proved negative. Septicemia cannot be ruled out, since a bacteriologic examination has been omitted. However, it appears improbable, since there was neither clinical nor anatomic evidence, particularly no changes in the heart muscle and kidneys.

Histologic examination of Case 3 showed no destructive but only mild fatty changes in the liver cells. The outstanding feature is the proliferation and the activity of the large mononuclear cells of the spleen, indicated by their conspicuous erythrophagocytosis, erythrorrhexis and hemosiderosis and the transportation of these cells to the liver. Similar pictures have been reported in two cases of icterus neonatorum by Lepehne,[7] from Aschoff's Institute, and by Schmincke[8] in a congenital icterus neonatorum.

The features which are common in these three cases reported are the jaundice and the fatal consequences. There are several points, however, which both clinically and anatomically call for a distinction. The first two cases showed a hemorrhagic condition which was not present in the third case. Anatomically, the first two cases showed severe liver changes and interruption of the continuity of the liver cells, which accounted for the severe jaundice. The third case showed no changes in the liver to warrant the jaundice, but signs of a hyperactivity of the reticuloendothelial cells of the spleen. The increased hemoglobin destruction in this case is sufficiently demonstrated by the histologic picture of the spleen, and there can be no doubt that the hemoglobin or its derivatives have been carried to the liver by the large mononuclear cells found in the sinuses of spleen and liver. There is, however, no histologic evidence of a bilirubin formation outside the liver. The yellow pigment granules in the siderocytes in the liver can certainly be considered as bilirubin crystals, but these findings are not conclusive for the assumption that bilirubin has been actually formed inside the cells, as it might have been merely engulfed by phagocytic activity. There are, however, two facts not considered as yet, which might prove helpful in this question. The kidneys of the first case showed a green color of the cortex, which became deep green after fixation in formaldehyd. This proved to be the same with the liver in the second case. The kidneys of the third case showed a deep yellow color of the medulla, which remained yellow even after several months of formalin fixation. Histologically, the first kidneys showed bile casts in the cortical tubules

7. Lepehne: Beitr. z. path. Anat. u. z. allg. Path. **65**:163, 1919.
8. Schmincke: Verhandl. d. deutsch. path. Gesellsch. **19**:173, 1923.

and impregnation of the tubular epithelium with bile. The third case showed bilirubin crystals in the tubules, and in the epithelial cells of the medulla. The intense jaundice of the medulla, with deposit of bilirubin crystals in the lumen and epithelial cells of the medullary tubules, contrasts with the bile casts and granular bile impregnation of the cortical tubules commonly found in severe jaundice of the adult, and it characterizes the jaundice of the kidneys in icterus neonatorum. It furnishes further evidence to conceive the jaundice in our third case as belonging to the type of icterus neonatorum. The reaction with formaldehyd, however, shows that the bilirubin in the third case is different from the bilirubin found in the first two cases and found in cases of obstructive jaundice. This different behavior of the bilirubin in icterus neonatorum was first demonstrated by Schmorl,[9] and generally Beneke [10] is given credit for having first recognized the dissimilar chemical nature of the bilirubin in icterus neonatorum. But long before Beneke's paper had been published, Warthin [11] briefly mentions in his textbook that hematoidin does not turn green in formaldehyd and recommends the reaction in the differentiation between bilirubin and hematoidin. The latter, however, is identical with bilirubin in its chemical constitution, but it is the bilirubin formed outside the liver.

From the foregoing considerations and the histologic evidence of increased blood destruction in the spleen, we now feel justified in conceiving our third case as a case of icterus neonatorum of anhepatocellular origin. Recent publications of Lepehne,[12] Hellmuth,[13] Knopfelmacher,[14] Williamson [15] and others have furnished evidence that the bilirubin in the serum of icteric new-born infants gives exclusively the indirect Van der Bergh's reaction, and have reached the same conclusion from another angle. The fatal consequence in the foregoing case of icterus neonatorum is sufficiently explained by the underweight of the child (birth weight 5 pounds) and by the infection with *B. coli.* Icterus neonatorum in itself is a physiologic condition, which of itself never proves fatal, but in babies of low vitality saprophytes of the intestinal tract may enter the blood stream and severe consquences may result. The icterus will be prolonged, because the liver is impaired in its function to excrete the bilirubin circulating in the blood. The conception is sustained by the observation of fatty changes in the liver in the case here reported.

---

9. Schmorl: Verhandl. d. deutsch. path. Gesellsch. **6**:109, 1904.
10. Beneke: Centralbl. f. Gynakol. **38**:847, 1914.
11. Warthin: Practical Pathology, Ann Arbor, George Wahr, 1911, p. 275.
12. Lepehne, G.: Monatschr. f. Geburtsh. u. Gynäk. **60**:277 (Oct.) 1922.
13. Hellmuth, K.: Monatschr. f. Geburtsh. u. Gynäk. **54**:340 (June) 1921.
14. Knoepfelmacher, W., and Kohn, C.: Monatschr. f. Kinderh. **22**:1 (Oct.) 1921.
15. Williamson, A. C.: Surg., Gynec. & Obst. **37**:57 (July) 1923.

There is still one point which I want to mention, without, however, drawing any further conclusions. In both cases with the severe liver changes, the family history revealed that icterus had occurred in previous children. In the first case three children were alive and one died with icterus ten days after birth. The second case is more significant. There the first child is alive and well. The next three children, including the case here reported, died with icterus eleven, fourteen and twenty-one days, respectively, after birth. It was on account of the unfortunate events in the two previous childbirths that the mother entered the hospital. The possibility that this case belongs to the group of familial icterus of new-born infants has to be considered. Cases of this type are by no means frequent, and exact clinical and anatomic observations are still scarce. Knoepfelmacher,[16] in a review on the subject of icterus gravis in the new-born, altogether questions the entity of familial icterus in the new-born. He claims that the so-called icterus gravis generally is to be considered as a septic jaundice, and that the peculiar repeated appearance in one family is merely incidental. In his opinion exogenous conditions, particularly unhygienic environment, have to be blamed as the cause of infections of the new-born. If these conditions persist, they will lead to a seemingly familial occurrence of septic jaundice. But more exact observations of the last years (Abt,[17] Yllpö,[18] Thorling,[19] Rolleston [20]) have established the fact that at least in these cases septicemia can be ruled out. In familial jaundice of the new-born, Rolleston maintains, maternal toxemia during pregnancy may play an important part. Thorling charges infections with vaginal germs, whereas Yllpö does not see any reason to separate the familial cases from the ordinary icterus neonatorum in their pathogenesis. The anatomic and histologic examination in the cases reported in the literature does not furnish much evidence to explain the jaundice. Generally, the liver did not show lesions to account for the icterus, with the exception of the eleventh case of Auden [21] in which death occurred twenty-two days after birth with universal fatty changes in the liver cells and considerable small round cells, Ashby's [22] case of twelve days duration, with necrosis of liver cells, and Pfannenstiehl's [23] patient, 21 days of age, with partial necrosis of liver cells. The reason why I hesitate to include the second case in the group of familial jaundice is that we have to

16. Knoepfelmacher, W.: Ergebn. d. inn. Med. u. Kinderh. **5**:205, 1910.
17. Abt, I. A.: Familial Icterus of New-Born Infants, Am. J. Dis. Child. **13**:231 (March) 1917.
18. Yllpö: München. med. Wchnschr. **65**:98, 1918.
19. Thorling, I.: Upsala Läkaref. Förh. **28**:1 (Oct.) 1922.
20. Rolleston: Practitioner, London **104**:1 (Jan.) 1920.
21. Auden: St. Barth. Hosp. Rep. **41**:139, 1905.
22. Ashby: M. Chron. **1**:25, 1884.
23. Pfannenstiehl: München. med. Wchnschr. **55**:2169, 1908.

rely only on the report of the mother. Since icterus in the new-born is so frequent, it might have been an accompanying symptom of a severe disease of the previous children which had not been recognized. As this doubt cannot be removed, we do not want to conclude anything regarding the pathogenesis of familial jaundice, particularly since the histologic examination of the liver in our case contrasts with the negative reports of other authors.

CONCLUSIONS

Our observations have led us to the conclusion that, in one group of fatal cases of jaundice in the new-born, the icterus has been due to a destructive process of the liver; in another group, however, it has to be considered as a prolonged icterus neonatorum of anhepatocellular origin. These conclusions warrant certain suggestions to the pediatrician. The early differentiation in cases of jaundice between the serious type of hepatic jaundice and the milder form of icterus neonatorum is of importance. It can be accomplished by the examination of the blood serum for bilirubin with the Van der Bergh test. In cases of icterus of hepatic origin, a rational therapy should be tried to protect the liver against further destruction by sustaining its glycogen reserve. The beneficial results of glucose transfusion in mushroom poisoning (Treupel and Rehorn [24]) and in toxemia of pregnancy (Titus and Givens [25]), which aim toward the same point, suggest the same therapy in cases of severe jaundice in the new-born.

24. Treupel and Rehorn: Deutsch. med. Wchnschr. **46**:509, 1920.

25. Titus, Paul, and Givens, U. H.: Intravenous Injections of Glucose in Toxemia of Pregnancy, J. A. M. A. **78**:92 (Jan. 14) 1922.

CORRECTION

Under "News and Comment," page 120, July issue, Dr. Frederick W. Schultz should read Dr. Frederick W. Schlutz.

Abstracts from Current Literature

Anatomy and Physiology

THE DUODENAL PYLORUS REFLEX. F. BARSONY and B. HORTOBAGYI, Orvosi hetil. **68**:320, 1924.

Based on their experiments on dogs, the authors come to the following conclusions:

The so-called duodenopylorus reflex, which was among the important principles of physiology for a long time, and which also gave the foundation to the pathology of stomach, pylorus and duodenum, does not exist. The explanations based on this reflex, are erroneous and entirely without value. The previous conception of a duodenopylorus reflex must be abandoned, and the theories built on the assumption of this reflex discarded.

ZENTAY, Baltimore.

THE RELATION OF THE SPEED OF SEDIMENTATION OF ERYTHROCYTES TO COLLOIDAL CONDITIONS OF THE PLASMA OF THE NURSLING. GEORG HILLE, Monatschr. f. Kinderh. **28**:137, 1924.

In recent years physiologists and clinicians have studied the so-called suspension stability of erythrocytes by estimating the speed of sedimentation in mixtures of plasma and sodium citrate. Attempts have been made to use this method as an aid in diagnosis. The idea seems to be that speed of sedimentation would depend on conditions of fibrinogen and globulin in the blood, which might be altered in disease.

Hille studied a number of normal infants of different ages and under different conditions. The blood was obtained by sinus puncture.

The time varies in different months. In the first month six hours were required; in the third and fourth month only from one to two hours were required, in the fifth month two hours, and in the sixth and seventh the time had gone to over three hours.

A starvation period of twenty-eight hours reduced the speed to some extent, probably by influencing the blood colloids.

GERSTLEY, Chicago.

CLINICAL STUDIES ON MUSCULAR TONE: (V) ON INTESTINAL TONE (CONTRIBUTION TO THE CLINICAL STUDY OF CHRONIC CONSTIPATION). ANTONIO GASBARRINI and FRANCESCO FLARER, Arch. di patol. e clin. med. **3**:1, 1924.

A rubber balloon was inserted through the rectum and connected with a tambour. Kymographic tracings were obtained of human intestinal movements and tone. Various drugs were given to the subjects of the test. Vagus stimulation (pilocarpin) increased and vagus inhibition (atropin) decreased intestinal tone. Sympathetic stimulation (epinephrin) showed less effect. The authors conclude that the intestine has an inherent mechanism, independent of the autonomic nervous system, for controlling the tone of its muscle.

THE PREPARATION OF INSULIN. MICHAEL SOMOGYI, EDWARD A. DOISY and PHILIP A. SHAFFER, J. Biol. Chem. **60**:31, 1924.

A method of extracting insulin from beef pancreas is described. The yield and strength of the resulting preparation is quite high. The active principle of the preparation probably is a protein (insulin protein). The authors made

use of certain physical properties of "insulin protein" in the extraction. Thus the protein is precipitated between p_H 4.4 and 5.8. The protein also is precipitated in acid solutions by the addition of sodium or ammonium sulphate. Sulphuric acid is used in the extraction because it causes less swelling of the pancreas hash, and makes the technic simpler.

A Note on the Technic of Heart Puncture in the Dog. E. W. Schultz, J. Biol. Chem. **60**:189, 1924.

The author has used heart puncture as a routine method of obtaining arterial blood in dogs. The technic involves entering the chest below the apex of the heart and shooting upward at an angle of 30 degrees to enter the left ventricle. This method is comparatively free from fatalities, as the larger coronary arteries are avoided.

Glycolysis in Bloods of Normal Subjects and of Diabetic Patients. Edward Tolstoi, J. Biol. Chem. **60**:69, 1924.

Blood was drawn, mixed with potassium oxalate, and kept under sterile precautions for a period of twenty-four hours. At intervals, samples were analyzed for glucose. The author found that the blood from diabetic patients had as great a glycolytic power as the blood of normal subjects. The glycolytic power in all cases was less at room temperature than at 37 C. (98. 6 F.).

Pathology and Bacteriology

Concerning the Mechanism of Acidosis in Anesthesia. Raymond Stehle and Wesley Bourne, J. Biol. Chem. **60**:17, 1924.

Experiments on rats showed an increase in the phosphorus of the liver, and decrease in the phosphorus in the muscle during ether anesthesia. Experiments on dogs showed that the phosphate content of blood plasma and the phosphate excretion in the urine increased after anesthesia. The increased acidity of the blood in ether anesthesia is due to phosphoric acid, which comes from the muscle and lodges in part in the liver. This phosphoric acid is later excreted in part.

Higgins, Cincinnati.

Congenital Stricture of the Duodenum. Marfan, Turquety and Debray, Le Nourrisson **12**:101 (March) 1924.

The most common locations of intestinal obstruction of congenital origin are (1) at the ampulla of Vater, (2) at the duodenojejunal junction and (3) at the ileocecal valve. The case reported was due to a congenital adenoma in the wall of the duodenum. The authors have not been able to find any report of a similar case in the literature. The infant was normal at birth but began vomiting on the second day. The vomiting continued with each nursing and the vomitus was yellowish green. Breast feedings were stopped for a while with slight improvement. Farina was tried, but the vomiting returned. There was marked constipation and stationary weight. The weight at birth was 2,600 gm. and at four months 2,750 gm. Roentgen-ray examination showed a dilatation of the stomach and the duodenal bulb, localizing the obstruction in the second portion of the duodenum. Operation could not be performed on account of an infection of the umbilicus. The baby died at the age of 6 months. At necropsy an adenoma about 5 mm. in diameter was found in the posterior wall of the duodenum, which almost entirely occluded the lumen of the intestine.

McClelland, Cleveland.

A Study on Bilirubinemia. Eugenia De Micheli, Arch. di patol. e clin. med. **42**, 1924.

The author, contrary to the work of German investigators, found bile pigments in normal serum of less than half of the cases examined. Bilirubin will enter the blood through the intestinal mucosa, as shown by the "Diazonium" reaction; but this is not the usual method by which bilirubin enters the blood.

Higgins, Cincinnati.

Colloid Inhibition of Anaphylactic Shock. Howard T. Karsner and Enrique E. Ecker, J. Infect. Dis. **34**:636 (June) 1924.

Guinea-pigs were sensitized by subcutaneous injections of 1 c.c. of a 1:20 dilution of horse serum. From twenty to twenty-five days later colloids were injected into the jugular vein on one side, followed by injection of the horse serum on the opposite side. The colloids employed were congo red, dextrin, glycogen, Witte peptone and kephalin.

The conclusions arrived at were as follows:

1. The suspensoid colloid congo red does not inhibit anaphylactic shock.
2. Although not definitely proved in these experiments, there is no doubt that the protein colloid Witte peptone is definitely inhibitory to anaphylactic shock.
3. Inhibition of anaphylactic shock by lipoid colloids, such as kephalin, is suggested by experiments in the hands of others and by the present study, but a critical examination of the method does not conclusively support this hypothesis.

Production of Mycelial Forms of Oidium Albicans in Carrot Infusion. A. A. Draper, J. Infect. Dis. **34**:631 (June) 1924.

A culture of Oïdium albicans was isolated from the stool of a patient with chronic diarrhea. In the stools, the mycelial forms predominated, often occurring as tangled masses of hyphae. As usual, the first subcultures yielded the yeast forms. An attempt was made to find conditions favorable for the formation of mycelial forms in cultures of Oïdium albicans. A few rudimentary filaments were formed in certain concentrations of acid and alkali on an agar medium. Only rudimentary filaments also were found on the solid carrot medium recommended by Guilliermond.

In an infusion of carrot, however, typical hyphae developed, and these closely resembled the forms found in the lesions of thrush.

Kennedy, Rochester, Minn.

Researches on Gastric Juice of Children From One to Twelve Years Old. Emil Klementsson, Acta Pediat. **3**:136 (Feb.) 1924.

Klementsson examined the gastric contents after an Ewald test meal, and found much less acid than in adults. The lowest values were in infants under 1 year. After this age the acidity increased up to the fourth and seventh years, and then remained constant throughout childhood. Acute gastro-intestinal upsets did not affect the secretion of acid, but in chronic gastro-intestinal disorders either total achylia was found or else the acid was very much diminished.

The author used the well known titrometric methods for ascertaining free hydrochloric acid and total acidity. He regrets that he used the Ewald test meal instead of a test meal of barley water which Chievitz has found more satisfactory.

Holt, Baltimore.

MICROBIC VIRULENCE AND HOST SUSCEPTIBILITY IN PARATYPHOID-ENTERITIDIS INFECTION OF WHITE MICE. IV. THE EFFECT OF SELECTIVE BREEDING ON HOST RESISTANCE. LESLIE T. WEBSTER, J. Exper. Med. **39**:879, 1924.

Mice were given mouse typhoid bacilli by stomach tube and the survivors were mated; this procedure was repeated in offspring for two consecutive generations. The resistance to the specific infection, mouse typhoid, and to a nonspecific poisonous substance, mercury bichlorid, was tested in the offspring of the survivors. The experiments were done under conditions which reduced the possibility of specific acquired immunity to a minimum. The author concludes: that, if mice surviving a lethal dose of mouse typhoid bacilli are inbred consecutively for a number of generations, the resulting offspring become progressively more resistant to mouse typhoid infection and to mercury bichlorid intoxication than similar control mice not so selected.

McCLURE, Evanston, Ill.

HUMAN HYPERSENSITIVENESS INDUCED BY VERY SMALL AMOUNTS OF HORSE SERUM. SANFORD B. HOOKER, J. Immunol. **9**:7, 1924.

A series of adults were tested intradermally with horse serum before the administration of toxin antitoxin (three L + preparation or the equivalent of 0.01 minimum lethal dose of horse serum) and six months afterwards. By an immediate positive reaction the author means the development within one hour of an irregular wheal surrounded by erythema. Before the injection, 10.5 per cent. showed positive reactions and after the injection 64.6 per cent. showed positive reactions. Of the ninety-six adults who gave negative skin tests before injection, twenty-six, or 27 per cent. showed immediate positive skin tests six months after the injections while seventy, or 73 per cent. showed delayed or negative reactions after the injections. This small dose of horse serum was less effective in establishing an allergic state than the larger doses of whole horse serum used in pneumonia, but no proof is available that the duration of such a state varies with the size of the dose. There is also no evidence that this induced allergy is of a degree that would render subsequent serum therapy dangerous. However, in view of the delay entailed by desensitization and the prejudice which would arise if unpleasant or dangerous reactions ensued, the author recommends that some other animal be chosen for the production of that antitoxin destined for use in toxin-antitoxin mixtures.

It is noteworthy that although the author gave toxin antitoxin to twenty-two persons with positive initial tests he noted no alarming symptoms.

GUY, New Haven.

EFFECT OF MECHANICAL AND INFECTIOUS FEVER ON GASTRIC ACIDITY IN INFANTS. ARVO YLLPÖ, Acta Pediat. **3**:213 (Feb.) 1924.

The author induced fever in a number of infants by a hot bath. Certain of these showed with great regularity a reduction in gastric acidity (increase in p_H) associated with this treatment. Similar findings were obtained in a few cases with the fever accompanying vaccinia. Yllpö thinks that mechanical overheating plays an important part in causing summer gastro-intestinal upsets. Parenteral infections act in the same way. In the first place, the alteration in acidity interferes with digestion, and, in addiiton, the lowered acidity in the stomach permits bacteria to survive that are ordinarily destroyed there by acid. These pass on to the intestine and set up pathologic processes there.

These observations furnish a rational basis for "acid milk" therapy which has become so popular of late. Yllpö thinks it should prove of still further value as a prophylactic.

HOLT, Baltimore.

PARADOXICAL SHORTENING OF THE COAGULATION TIME OF THE BLOOD AFTER INTRAVENOUS ADMINISTRATION OF SODIUM CITRATE. NATHAN ROSENTHAL and GEORGE BAEHR, Arch. Int. Med. **33**:535 (May) 1924.

The authors state that this striking phenomenon of shortening the coagulation time of the blood, the exact opposite of what occurs in vitro, was made the subject of a detailed experimental study, in order to ascertain what changes were induced by sodium citrate in the complicated mechanism of blood coagulation. For this purpose the effect on each factor involved in coagulation was studied individually. Detailed accounts were given of the material and technic, with a discussion by the authors of observations on the effect of sodium citrate on calcium, fibrinogen, antithrombin cytozyme, and serozyme (thromboplastic substance and prothrombin) blood platelets and the mobilization of blood platelets.

Because of the great part played by blood platelets in coagulation the study was subjected to two series of experiments: 1. Effect of sodium citrate on animals that normally do not possess any blood platelets comparable to the mammalian. For this purpose ducks were used. 2. On human beings in whom because of disease there existed a marked numerical deficiency or disease of the platelets; for this purpose two patients were selected (1) essential thrombopenic purpura (the so-called purpura hemorrhagica); (2) congenital hemophilia. In conclusion the authors believe that the shortening of the coagulation time after injection of sodium citrate in normal persons or animals is due to some influence on the blood platelets. That this is not a direct destruction is proved by the test tube experiment, and by the fact that the maximum shortening of coagulation time does not occur simultaneously with the maximum reduction in platelets, but follows from ten minutes to one hour later.

Although the coagulation time of the blood is often materially shortened, no tendency to intravascular thrombosis has ever been observed. The real danger to be guarded against is a too hasty injection. In hemorrhagic blood disease, the use is strictly contraindicated. With these observations as a basis, the slow intravenous injection of large doses of sodium citrate up to 5 gm. has been successfully employed in arresting hemorrhage due to gastric ulcer, typhoid fever, pulmonary tuberculosis and other bleeding conditions that are not accompanied by diminution or diseases of the blood platelets.

LOEBER, New Orleans.

HUMAN HYPERSENSITIVENESS TO WHOLE HORSE SERUM AND SERUM GLOBULINS FOLLOWING DIPHTHERIA TOXIN-ANTITOXIN INJECTIONS. ITS IMPORTANCE. WILLIAM H. PARK, J. Immunol. **9**:17, 1924.

Two series, one of children and one of adults, were tested intradermally with either horse serum or antitoxin globulin solution. The reactions to both solutions were almost identical. By an immediate positive reaction the author means the development within from fifteen to twenty minutes of an irregular wheal surrounded by erythema. In the first group, comprising 116 children injected one year previously with three doses of an 0.1 L + mixture of toxin-antitoxin (or the equivalent of 0.0006 c.c. of horse serum) 27.5 per cent. gave positive reactions. In the second group of ninety children, who probably had not had any previous horse serum, 11 per cent. gave positive reactions. In the second series of thirty adults who had received (time interval not noted) three injections of 3 L + toxin-antitoxin mixture, 33 per cent. gave positive reactions, while in the control series of adults who had not previously received horse serum injections only 19 per cent. gave positive reactions. Another series of sixteen children were tested at varying periods from 15 to 56 days after an injection of antitoxin globulin solution (1,500 to 3,000 units). Of these,

62.6 per cent. showed skin hypersensitiveness. The author concludes that toxin-antitoxin contains sufficient serum globulin to sensitize moderately a certain proportion of individuals receiving three injections and that larger doses of globulin will sensitize a larger proportion of people. But he does not consider this degree of induced hypersensitiveness of peril if later serum injections become necessary. He gave antitoxin intramuscularly to thirty children who had had antitoxin about four weeks previously and who gave positive skin reactions. Many of these children developed fever and a local or generalized rash, but none of them showed alarming symptoms. He gave antitoxin intravenously to twelve children showing small positive skin reactions, without alarming symptoms. One child did develop cyanosis and dyspnea, which were readily controlled by epinephrin. Although the author states his belief that most of the few deaths following toxin-antitoxin have occurred on first injection, he does not advocate the general use of a previous intracutaneous test, and he concludes that subcutaneous and intramuscular injections of whole serum or antitoxin globulin solution are quite safe without waiting for the result of a skin test. He now feels confident that if there is no history of asthma or sign of status lymphaticus, intravenous injections in such circumstances are safe if given slowly and carefully.

HEMAGGLUTINATION IN HORSES. L. S. N. WALSH, J. Immunol. **9**:57, 1924.

Walsh has found that autohemagglutination in horse blood is associated with the early phases of coagulation and that the autohemagglutinins and agglutinogens deteriorate on standing. Although he can demonstrate no distinct blood groups by hemagglutination he finds certain suggestive irregularities. He does not find that either iso-hemagglutinins or autohemagglutinins are absorbable. Small amounts of calcium chlorid increase while large amounts inhibit agglutination. Citration of the blood slightly inhibits, whereas decalcification by ammonium oxalate does not inhibit auto-agglutination.

BLOOD INTERRELATIONSHIP OF HORSES, ASSES AND MULES. L. S. N. WALSH, J. Immunol. **9**:48, 1924.

Walsh finds that the serum of the ass agglutinates the erythrocytes of the horse but not those of the mule. It hemolyzes the erythrocytes of both horse and mule. The serum of the mule, however, does not alter the erythrocytes of the horse. The blood of the mule resembles that of both horse and ass, the serum is like that of the horse, and the corpuscles like those of the ass.

OBSERVATIONS ON BACTERIAL ANAPHYLAXIS WITH PNEUMOCOCCUS. HANS ZINSSER and T. B. MALLORY, J. Immunol. **9**:75, 1924.

Zinsser has demonstrated by the uterine contraction method, active and passive sensitization of the guinea-pig with pneumococcus protein.

TUBERCULIN HYPERSENSITIVENESS WITHOUT INFECTION IN GUINEA-PIGS. HANS ZINSSER and S. A. PETROFF, J. Immunol. **9**:85, 1924.

Using repeated injections of dead tubercle bacilli, the authors have produced in the guinea-pig skin sensitiveness of the tuberculin type.

STUDIES ON ANTI-MENINGOCOCCUS SERUM. 1. PRODUCTION OF SERUM. I. R. MØRCH, J. Immunol. **9**:25, 1924.

Using the only pathogenic type of meningococcus found in Denmark, Mørch has studied the antibody formation in immunized horses. He finds no correlation between the quantities of different antibodies at the same time, nor does he find the time interval after the last injection of antigen to be the same for the optimum yield of different antibodies. The optimum time of bleeding varies with the antibody chosen as the gage of therapeutic activity. Daily injections of manganese chlorid seemed to have a stimulating effect on antibody formation.

GUY, New Haven.

TUBERCULOSIS OF MAMMALIAN TISSUE IN VITRO. ALEXANDER A. MAXIMOW, J. Infect. Dis. **34**:549 (June) 1924.

Maximow cultivated tubercle bacilli with the lymphoid tissue of mesenteric lymph nodes, the omentum and the common loose intermuscular connective tissue of adult rabbits. Two strains of bacilli of the human type were isolated from sputum and used in the experiments; one was highly virulent for guinea-pigs, the other was of low virulence. The tissue cultures were prepared according to Maximow's technic and after from three to five days they were inoculated with bacilli. Examinations were made after from two to three weeks, with special fixing and staining methods.

Though, as is well known, contamination of tissue cultures by saprophytic micro-organisms results in a rapid destruction of the tissue cells, in the presence of tubercle bacilli the tissue cells not only do not perish, but they display a series of reactive changes, partly undoubtedly of progressive character, which represent an exact duplication of the specific tuberculous inflammatory process, as it is found in the organism.

In the cultures of lymphoid tissue the reticular cells are the most active elements. They are mobilized, hypertrophy, divide and become transformed into large polyblasts (Maximow), epithelioid cells, actively phagocytizing the tubercle bacilli. The epithelioid cells assemble in clusters, corresponding to tubercles. Many of the cells fuse together and in this way the giant cells of the Langhans type are produced.

The lymphocytes hypertrophy, become transformed into polyblasts, later sometimes acquire an epithelioid character and join the giant cells in the process of tubercle and giant cell formation. When the lymphocytes become epithelioid in character they become actively phagocytic.

The tubercle bacilli, engulfed by epithelioid cells, are either digested, leaving in the protoplasm a peculiar yellow pigment, or they multiply excessively in the body of the phagocytes, overcrowding the protoplasm. Such cells may retain their vitality for a long time. In the giant cells the digestive power of the protoplasm is probably far higher and therefore the number of intracellular bacilli usually does not increase excessively.

The typical end result of the tuberculous process in the organism, the caseation, also can be observed in the cultures. In the larger clusters or tubercles, the epithelioid cells degenerate, showing diffuse accumulation of small, evenly divided fat droplets, karyorrhexis and karyolysis, and finally detritus with occasional bacilli remains.

Similar facts can be observed in the inoculated cultures of the omentum and simple connective tissue. In the first, the resting wandering cells are mobilized to epithelioid polyblasts, engulf tubercle bacilli and form the typical tubercles. In the second, although the bacilli usually do not penetrate into the tissue, the resting wandering cells hypertrophy, are transformed into epithelioid cells and even small atypical giant cells are formed through amitosis of their nuclei. Except perhaps in the case of the omentum, the fibroblasts do not take any part in the formation of tubercles and giant cells. They proliferate and assume an embryonic character, but remain sharply separated from the other elements.

KENNEDY, Rochester, Minn.

Nutrition

MIXED DIET DURING THE FIRST YEAR OF LIFE. I. JUNDELL, Acta Pediat. **3**:159 (Feb.) 1924.

Jundell reports thirty-one infants to whom he fed a mixed diet from the age of 6 months onward, with noticeable success. His diet included fish, meats, eggs, potatoes, vegetable purées, bread, etc. He gains the impression that digestive disturbances are rarer on this diet than when exclusive milk feeding is continued longer.

HOLT, Baltimore.

RELATIONS OF REACTION OF INTESTINAL CONTENTS TO DIET AND FLORA. PAUL HUDSON and LELAND W. PARR, J. Infect. Dis. **34**:621 (June) 1924.

Series of white rats were fed with various diets for ten days, and they were then killed and the contents of the cecum and colon separately emulsified in sterile salt solution and examined in regard to reaction and flora.

It was found that a diet containing sufficient carbohydrate to effect a complete turnover from a heterogeneous, gram-negative type of flora in rats fed on high protein and stock diets, to a flora markedly simplified and gram-positive, induced coincidently a change in the hydrogen-ion concentration from nearly neutral to distinctly acid.

In rats fed on high carbohydrate diet this acid environment was much more marked in the cecum than in the colon. In the same animals, however, even the contents of the descending colon were more acid than those of the rats fed on a high protein or stock diets.

Intestinal spirochetes were found in a larger number of rats on a high protein and stock diets, and in the cecum of these rats to a greater degree than in the descending colon, coincident with putrefaction and less acidity.

KENNEDY, Rochester, Minn.

GROWTH AND REPRODUCTION UPON SIMPLIFIED FOOD SUPPLY. IV. IMPROVEMENT IN NUTRITION RESULTING FROM AN INCREASED PROPORTION OF MILK IN THE DIET. H. C. SHERMAN and H. L. CAMPBELL, J. Biol. Chem. **60**:5, 1924.

The authors compare the growth and reproduction in rats who were kept on specified diets of milk and wheat. Diet A consisted of one-sixth dry milk and five-sixths ground whole wheat. The author had previously found that this was an adequate diet, and that rats would grow and reproduce over as many as eight generations. Diet B consisted of one-third dry milk and two-thirds ground whole wheat. This latter diet proved to be a much better diet in that the rats gained more in weight, and were larger at all ages, although the same number of calories were taken in both diets. The rats on Diet B reproduced earlier; had a longer duration of reproductive life, and reproduced much more rapidly. There is a large zone between adequate and optimum nutrition.

HIGGINS, Cincinnati.

THE EFFECT OF MENSTRUATION ON LACTATION. A. F. CANELLI, Le Nourrisson **12**:92 (March) 1924.

Six hundred and ninety nursing mothers and twenty-five wet nurses were observed by Canelli in the prophylactic dispensary at Turin. In 170, or 25 per cent., menstruation came on during the nursing period, being somewhat more frequent in the primipara and the secundipara. The average time of appearance was four and one-half months after confinement. In the great majority of cases, once menstruation reappeared it was of the same duration as before pregnancy. Of the babies observed fifty, or 30 per cent., showed loss in weight

during the time the mother was menstruating. Other symptoms noted were sleeplessness, restlessness and loss of appetite. In only twenty-six cases did the menstruation seem to be responsible for diarrhea in the infant. The loss in weight, as well as the diarrhea, was of little consequence and such minor disturbances do not warrant any interruption in nursing. Only when the menstruation is prolonged and occurring at more frequent intervals is the well being of the baby likely to suffer.

McClelland, Cleveland.

Prenatal Conditions

Congenital Peripheral Resistance: Its Causative Relation to the Precocious Hypertensive States. Eli Moschowitz, Arch. Int. Med. **33**:566 (May) 1924.

The author reviews at length the literature on nephritis associated with hypertension, and by hyptertension with early arteriosclerosis, nephritis and narrow aorta. He shows from his citations that cardiorenal disease, especially in the young, is frequently associated with narrow aorta.

He deplores the fact that, in a review of the literature on hypertensive nephritis in childhood, the size of the aorta is ignored. The author states that whatever the significance of narrow aorta may be, the fact remains that (1) there exists a uniform diminution in size of the aorta from the root to the iliac bifurcation; (2) the size of the aorta is fairly uniform for the age and height of the person; (3) an aorta may be regarded as definitely narrow when it is at least from 5 to 10 mm. smaller at a point 1 cm. above the root than the mean average compiled from the Beneke, Scheel and Kaufman tables. Several authors are quoted to substantiate the fact that a maldevelopment of a hypoplastic nature is a factor in juvenile nephritis. He thinks this may also explain cases of familial nephritis, and cites several cases of other authors to corroborate his views. He cites a case from Hill of chronic interstitial nephritis with hypertension in a child with infantilism, and after quoting four cases of arteriosclerosis in children all suffering from hypoplasia, and the fact that familial tendency of juvenile arteriosclerosis is commented on by most observers, he states that the evidences, while few, are suggestive, and the deficiencies in our observations are only too evident, and urges that more work be done so as to attain a correct knowledge of the statistical relationship of congenital peripheral resistance to hypertension and its sequences, arteriosclerosis and nephritis. His conclusions are briefly: 1. The immediate cause of hypertension is unknown. 2. Among remote causes, psychic factors play an important rôle. 3. Peripheral resistance is of importance in the causation of hypertension and its consequences, arteriosclerosis and nephritis. 4. There is evidence that a congenital peripheral resistance, either in the form of congenital stenosis of the isthmus of the aorta (aorta angusta), may be the cause of hypertension, arteriosclerosis and nephritis. This may account for the etiology of some cases of juvenile or presenile arteriosclerosis and nephritis and some cases of familial nephritis.

Loeber, New Orleans.

Acute Infections

Recent Advances in the Control of Diphtheria. R. H. Mullin, Canad. M. A. J. **14**:398 (May) 1924.

This is an excellent review of the advances which have been made in the diagnosis and treatment of diphtheria. The importance of the Schick test and toxin-antitoxin immunization is stressed.

The work of Valdeman Bie of the Blegdam Hospital, Copenhagen, is reviewed in detail. This investigator groups his cases into four groups according

to the severity of the case. The outstanding features of this report are the low mortality rate (0.9 per cent.) and the large dosages of antitoxin. The following dosage is advised.

Group 1. Membrane not quite covering tonsils, from 4,000 to 8,000 units on admission. Membrane covering tonsils, from 16,000 to 20,000 units.

Group 2. Membrane extending beyond tonsils, 32,000 units under 10 years of age; 40,000 units over 10 years of age. Repetition of dosage if membrane extends.

Group 3 and 4. Severe cases, 80,000 units under 10 years; 60,000 units in twelve hours and 20,000 units in twenty-four hours, total 160,000 units; 10 years or over 100,000 units on admission, 80,000 units twelve hours later and 40,000 units twenty-four hours later, total 220,000 units.

Largest single dose was 196,000 units and largest total amount 350,000 units.

Intramuscular or combined intravenous and intramuscular methods are advised.

Roemers intracutaneous test for determining the virulence of diphtheria bacilli shortens the quarantine period of carriers from forty-eight to seventy-two hours and is of great value.

MOORE, Omaha.

SPECIFIC PROPHYLAXIS OF WHOOPING COUGH. ZOLTAN ROKAY, Orvosi hetil. **68**:237, 1924.

An auto group vaccine prepared by cough spray has been used on Schottmüller or Bordet-Gengou culture plates. Three injections of from 0.5 to 1.0 c.c. of the vaccine have been made in four days intervals. Of 125 children exposed to infection, only two contracted whooping cough. The writer thinks that these results with the auto group vaccine are encouraging and should be tried by others.

ZENTAY, Baltimore.

ON DYSENTERY AGGLUTINATION IN CHILDREN. PAUL WIDOWITZ, Acta Pediat. **3**:101 (Feb.) 1924.

Widowitz was able to culture dysentery bacilli in only 10 per cent. of cases clinically positive, but could always demonstrate agglutinins in the serum for either Flexner, "Y" or Shiga types after the first week of the disease.

He thinks that "normal agglutinins" in normal persons (e. g., those who agglutinate bacilli in dilutions no higher than 0.1) indicate a past dysentery infection which may have escaped notice. His evidence for this is: (1) the new-born show no such agglutinins; (2) no such agglutinins were found in a series of infants under 1 year who had been closely observed and had been diarrhea free. Subsequently all these infants contracted dysentery and developed agglutinins; (3) in a large number of normal persons of all ages, 86 per cent. of those with a history of diarrhea showed such agglutinins, while only 40 per cent. of those with negative history of diarrhea agglutinated. He studied the age at which these agglutinins appeared in "normal" persons.

	Under 4 mos.	4 mos. to 2 yrs.	2 to 5 yrs.	5 to 11 yrs.	11 to 14 yrs.	Over 14 yrs.
Per cent. showing positive agglutination	0	3.7	44	68	86	98

He concludes that in civilized countries practically all adults have harbored dysentery bacilli.

He draws an analogy between dysentery and tuberculosis, and between the "normal" agglutination reaction and the tuberculin reaction, suggesting that the former may also indicate a latent infection.

Two points in this work seem particularly worthy of comment. Widowitz points out the bad prognostic significance of a falling agglutinin titer in the serum. Several of his patients showed this shortly before death, and in the blood necropsy no agglutinins could be demonstrated.

Widowitz also describes a phenomenon by which dysentery may often be diagnosed serologically as early as the third day. When the agglutination tube is set up, the bacteria, instead of settling out in a circular mass, tend to settle in irregular, concentric starshaped masses. This phenomenon occurs several days before macroscopic agglutination. It can only be obtained in first infections (e. g., in infancy).

HOLT, Baltimore.

Chronic Infections

SUGGESTED CLASSIFYING OF CONGENITAL SYPHILIS INTO A MALIGNANT AND A BENIGN FORM AND TREATMENT. OSCAR HERZ, Monatschr. f. Kinderh. **28**: 159, 1924.

In treating congenital syphilis one factor has been overlooked, namely, the treatment of the parents with antisyphilitic medicaments. Herz suggests that in cases where parents have been insufficiently treated, the spirochetes have acquired a certain immunity to treatment and hence will be far more malignant to a child than the spirochetes of untreated parents.

The child with congenital syphilis carries depots of spirochetes which swarm into the blood on commencing antisyphilitic therapy. Inactive syphilis can, by a small dose of neoarsphenamin, develop manifest symptoms. Thus a dose of neoarsphenamin to a child with the so-called malignant type might be fatal. For that reason, Herz suggests a very mild treatment in the form of mercury ointment or mercury by mouth for those children whose parents still have the disease.

Herz's article is purely theoretical, but he gives us something to consider and he suggests by way of experiment, inoculating a rabbit thus: (1) from a nursling with malignant syphilis, (2) from a nursling with benign syphilis.

GERSTLEY, Chicago.

ON THE RÔLE OF THE GLOBULIN AND ALBUMIN OF THE SERUM IN THE WASSERMANN REACTION. LUIGI FONTANA, Arch. di patol. e clin. med. **3**:154, 1924.

The proteins, globulins and albumin of the serum are separated by the use of carbon dioxid and the rôle of each in the Wassermann reaction was studied. The author concludes from his and other author's researches that the primary agent of the positive Wassermann reaction is in the seroglobulin (euglobulin and pseudoglobulin). In serums which are not strongly positive it is the euglobulin, alone.

HIGGINS, Cincinnati.

SIGNIFICANCE OF THE PIRQUET TEST. A. B. MARFAN, Nourrisson **12**:73 (March) 1924.

In the five years from 1914 to 1918, 2,784 Pirquet tests were done on the children on Marfan's service; the children varied in age from early infancy up to 15 years. Of these tests, 949 were positive and 1,835 negative. In infants under 1 year only 10.5 per cent. reacted positively. At 5 years, over 50 per cent. were positive and at 15 years practically 80 per cent., thus proving the increased frequency of tuberculous infection with increasing age. On the basis of these statistics Marfan advances the following propositions: (1) tuberculous infection is practically never congenital; (2) the infection is usually contracted in early years of life; (3) these early infections, when recovered from, establish an immunity which is found in most adults. This immunity seems to follow especially the tuberculous adenitis which is so common in children. For this reason the excision of tuberculous glands in children is not justifiable.

Tuberculosis in infants under 1 year is almost uniformly fatal. Hence the importance of guarding these young infants against exposure. In older children more benign forms are encountered, especially that form usually called scrofula. The severe forms are due to massive or frequently repeated infections.

HYDROCELE ASSOCIATED WITH CONGENITAL SYPHILIS. NECROPSY. SALES and VALLERY-RADOT, Nourrisson **12**:138 (March) 1924.

The authors believe that certain cases of congenital hydrocele are due to syphilis, and consider themselves fortunate in being able to report such a case with the necropsy findings.

The baby, aged 3 months, had the usual signs of congenital syphilis; Generalized adenopathy, snuffles, rhagades, enlarged spleen, etc. Wassermann reaction on blood, spinal fluid and on the fluid from the hydrocele were all strongly positive. In spite of treatment with neoarsphenamin the baby lost weight and died from athrepsia. The necropsy showed a marked thickening of the tunica vaginalis, especially on the right side. The right testicle was hypertrophied and very hard. The right epididymis was larger than the left. Histologically, the sections showed swelling of the endothelium and vascular lesions, with perivascular infiltration of lymphocytes characteristic of syphilis.

Internal Diseases

ACUTE LYMPHATIC LEUKEMIA IN INFANCY. P. GAUTIER and A. THEVENOD, Nourrisson **12**:1, 1924.

Acute lymphatic leukemia is rare in children under 2 years. In 1909, Babonneix and Tixier reviewed the literature and published thirteen cases from French, German and English literature. Since then, Gautier and Thevenod have found reports of seven additional cases, and give a detailed report of their own case, which occurred in a baby, aged 12 months, and began six weeks after the onset of whooping cough. The authors point out that lymphatic leukemia supervening on whooping cough is not infrequent, citing two other cases in addition to their own.

They direct attention to the well known lymphocytosis present in whooping cough and the concomitant hypertrophy of the lymphatic glands, and believe that acute lymphatic leukemia is merely an exaggerated type of the same condition. "Between whooping cough, with its atypical lymphocytosis and adenopathy and acute lymphatic leukemia we believe there is no essential difference."

The enormous leukocytosis usually found in lymphatic leukemia is not necessarily characteristic of the affection. In the author's own case the white blood cells were never higher than 17,000, and a few days before death they went down to only 3,100. Other cases are cited with counts of 8,000, 3,000 and 10,000 respectively. More important than the number of cells is the character of the cells, the serious condition of the patient, the enormous hypertrophy of the lymphatic glands and spleen and the fatal outcome.

Radiotherapy was tried and although definite improvement was evident for a time, with diminution in the lymphocytosis and the size of the glands, death was not prevented. In fact roentgen-ray treatment may be definitely harmful by acting unfavorably on the bone marrow, producing hemorrhages and necrosis, with a marked anemia and thus reducing the resistance of the patient. Necropsy findings are recorded.

MCCLELLAND, Cleveland.

CONTRIBUTION TO THE STUDY OF THE HYPOPHYSEAL SYNDROME, HYPOPHYSEAL INFANTILISM AND DIABETES INSIPIDUS, THE METABOLISM OF WATER AND CHLORIDS. LUIGI FERRANNINI, Arch. di patol. e clin. med. **3**:113, 1924.

The case of a boy, aged 14, with diabetes insipidus and infantilism is reported. The literature regarding this hypophyseal syndrome is extensively reviewed. Observations were made on the water and chlorid balance under various experimental conditions. Following the giving of 10 gm. of sodium chlorid three times daily, the water balance was essentially unchanged, and some chlorid was retained in the body. A low chlorid diet also did not affect the water balance, but chlorids in excess of the intake were excreted. One hundred grams of honey caused the excretion of larger amount of water than ingested. The specific gravity was unchanged in each case. The efficacy of several preparations from the pituitary gland in relieving the polyuria was tested; the only preparation causing appreciable diminution of the volume of urine was an extract of the posterior lobe given hypodermatically.

HIGGINS, Cincinnati.

CONCERNING THE PHYSICAL DEVELOPMENT OF THE CHILDREN OF TUBERCULOUS PARENTS. JULIUS PEIZER, Monatschr. f. Kinderh. **28**:146, 1924.

Peizer divided his material in the children's department of the tuberculosis dispensary of Berlin into four groups: (1) those whose parents were both dead of tuberculosis, (2) those whose fathers died of tuberculosis, (3) those whose mothers died of tuberculosis, (4) those neither of whose parents have tuberculosis.

This material Peizer analyzed as regards height, weight, age and various chest measurements.

The results of this survey were rather surprising. As regards height, two-thirds of the children in all groups were about average. If anything, the predisposed children were in some cases superior to the normal children. The same applies to the figures concerning weight. The failure of the normal children to be superior to the predisposed ones is probably due to the fact that the normals seen were the weaklings of the family and hence sent to the dispensary for examination. In chest measurements however, the number of the narrow chested was considerably more in the predisposed than in the controls, and seemed to occur more in Group 3.

However, as the percentage of the narrow chested children was considerably higher in the control group than either Group 2 or 3, the writer concludes that the narrow chest is not a result of tuberculosis, but simply a morphologic type suggesting general physical weakness.

GERSTLEY, Chicago.

A NEW METHOD FOR X-RAY PHOTOGRAPHY IN STRICTURES OF THE ESOPHAGUS. ARTHUR POLLERMAN, Orvosi hetil. **68**:245, 1924.

A long rubber tube is introduced into the esophagus with the help of a sound. The walls of the tube are thin and impregnated with lead, the end is closed so that the tube can be pumped up through the mouth. The thin rubber lying closely to the wall of the esophagus shows the exact shape of it. In very bad strictures, where the tube cannot be introduced, bismuth is used, suspended in oleous-gummous mixture, which gives better results than watery suspensions.

ZENTAY, Baltimore.

EXPERIMENTAL CHRONIC GLOMERULONEPHRITIS. LOUIS LEITER, Arch. Int. Med. **33**:611 (May) 1924.

The author presents a critical review of the subject of experimental nephritis. He endeavors also to classify the terms dealing with chronic pathologic lesions of the kidneys, and concisely states the object of his study to be the production

of chronic glomerulonephritis in an experimental animal. The toxic agents selected for producing this condition are known to produce this kidney lesion in the human being. Scarlet fever, diphtheria, bacterial endocarditis and severe sore throat are often followed by glomerulonephritis. The rabbit which he, as well as others whom he cites, has used as the experimental animal, he deems as probably unsuitable for this purpose because it does not react as does the human being to the agents that can injure the glomeruli. After numerous experiments with methods which were calculated to damage the circulation within the glomeruli and introduce infection at the same time, he concludes his attempts were a failure as they did not produce changes in the kidneys which could be interpreted as those of chronic glomerulonephritis.

HEMATOPORPHYRINURIA AS AN INDEPENDENT DISEASE ("HEMATOPORPHYRIA") AND AS A SYMPTOM OF LIVER DISEASE AND INTOXICATIONS. FRANCIS HARBITZ, Arch. Int. Med. **33**:632 (May) 1924.

The condition is one still shrouded in mystery, belonging to the indefinite group of autointoxications. Two varieties are described, the acute and chronic forms.

Although the presence of hematophorphyrin in the urine is an essential feature, the author states that we do not really know what hematoporphyrin really is and where and whereof it is formed. Its presence in the urine is demonstrated by the spectroscope. The theory is advanced that it is formed in the liver, bilirubin furnishing the material.

The case contributed by the author falls into the classification of the acute variety.

The chronic or congenital variety is described but the author states it is rare, and even of doubtful identity, this latter variety is not associated with actual toxic phenomena, but with photosensibilization, manifested by cutaneous lesions after exposure to light. In both varieties the disease manifests itself only in those persons exhibiting a peculiar constitutional fitness for the disease.

AN ANATOMIC AND CHEMICAL REPORT ON A UNIQUE CASE OF MYELOMA. A. W. MEYER and F. A. CAJORI, Arch. Int. Med. **33**:581 (May) 1924.

The author reviews the literature to date and notes the rarity of the condition, and urges even the anatomist to record incidental cases so as to aid the clinicians in recognizing these cases before death. A complete and detailed description of the gross and histologic specimen is given. Signs and symptoms as obtained from the history of the case, and such additional diagnostic signs from the gross appearance of the cadaver were recorded, these being given so as to aid the clinician to diagnose this rare condition antemortem. The author recommends the use of the roentgen ray as an aid in antemortem diagnosis because of the lesions in the bones.

The chemical findings note that the calcium liberated in the destruction of the bone tissue is thought by the author to be rapidly and in a large part excreted from the individual, and in relatively small amounts only, deposited in other parts of the body, and the large tophi deposits on fingers proved to be urates, not calcium; though the bones were soft even to the point of fracture and the ratio of the calcium and PO_4 in the bone samples is not far from 400 to 570, the ratio existing in normal bone.

THE METABOLISM-PULSE RATIO IN EXOPHTHALMIC GOITER AND IN LEUKEMIA. RICHARD GEORGE MINOT, HOWARD JAMES MEANS and CONSTANCE HOPKINS, Arch. Int. Med. **33**:576 (May) 1924.

This paper is Number 8 of a series of studies in metabolism from the Harvard Medical School and allied hospitals. The study is made to answer the self imposed hypothetic questions: what causes the rapid pulse in hyperthyroidism? Is it solely dependent on increased metabolic rate, or is there invariably some other factor that produces tachycardia?

The question is answered indirectly by comparing the relation between the basal metabolism and basal pulse rate in hyperthyroidism with that in leukemia, two conditions without fever. These two afebrile morbid states are conspicuously characterized by an increase rate of heat production.

After statistical study from a plat made of the basal metabolism (ordinates) against basal pulse rate (abscissae) for 126 cases of exophthalmic goiter covering 180 observations, and 71 cases of chronic leukemia in 110 observations there was noted a high degree of correlation between the data for basal pulse rate and basal metabolism in both diseases.

These observations indicate that, for a given basal metabolism there is the same degree of pulse elevation in chronic leukemia as there is in exophthalmic goiter, and that certain symptoms, as sensation of warmth, increased sweating and flushed, moist skin, symptoms often observed in leukemia patients as well as exophthalmic goiter, are believed to be due to increased heat elimination, a direct expression of an increased metabolic rate, and that the symptoms of loss of weight, excessive appetite and dyspnea is an attempt on the part of the organism to compensate for the increased heat production.

CALCIUM TREATMENT FOR EDEMA. REED ROCKWOOD and CHARLES W. BARRIER, Arch. Int. Med. **33**:643 (May) 1924.

A review of the literature on the effects of various salts both on normal infants and adults, as well as on cases of edema of nephritis, idiopathic edema of the nephrosis type, of edema of cardiac origin, in ascites due to cirrhoses of the liver, and in pleurisy with effusion.

Seven cases are cited by the authors to show the effect of large doses of calcium given by mouth on massive edema of diabetic and nephritic origin. The good results, especially in the diabetic cases as the authors state were spectacular. In the few instances in which small doses of calcium were used little or no effect was observed. In some of the cases edema was reduced by calcium lactate, in others calcium chlorid seemed more effective. It was noted also that large doses of calcium do not seem to increase the amount of serum calcium. In one case of chronic glomerular nephritis, renal function was definitely improved as the edema subsided. This observation had been noted by other investigators. The authors believe that the high calcium content of milk may explain its diuretic action, and thus account for its popularity in the treatment of acute nephritis, and suggest that if calcium is the cause of the beneficial action of milk diets in nephritis, it would seem logical to prescribe diets in which the protein, salt, fluid, and caloric value have been properly adjusted, and then to give the necessary amount of calcium in addition, rather than to employ milk alone. They advance the hypothesis that calcium in the combinations in which it is present in milk may be absorbed at a different rate than when it is given as the pure salt. In one case of diabetic edema the basal metabolism rate rose during the administration of calcium from 13 to + 57 in twenty-five days. A similar dose of calcium did not produce a change in the basal metabolic rate of a normal person, nor in the other cases of edema discussed.

THE HISTOGENESIS AND NATURE OF GAUCHER'S DISEASE. THEODORE R. WAUGH and D. S. MACINTOSH, Arch. Int. Med. **33**:599 (May) 1924.

This study gives the results of the findings and observations of an early case of Gaucher's disease, as indicated from the clinical history of the case, and the pathologic examination of the spleen.

The disease occurred in a Jewish girl, aged 5 years, who had been under observation for enlarged spleen for about two years before surgical interference was resorted to. A detailed account of the case history, physical examination, operation, gross and histologic findings of the spleen is given. The authors believe that one general outstanding feature of Gaucher's disease is that the disease is one of the hematopoietic system. Only those organs are involved which possess hematopoietic activity. This fact has hitherto been submerged in the detailed study of the cells themselves. The fact that the lesion is located in the reticuloendothelial tissue or system of the body, the relation of which to the blood formation is now well recognized, is looked on as a matter of importance; the location being one to be looked on as related to some type of hematopoietic activity. The racial, familial, and congenital nature of the disease is taken as suggestive of a condition which either exists deep within the organic constitution of the person, or is concerned with the earlier development in still embryonic processes. Stress is laid on the observation that the origin and development of the specific Gaucher's cells are from the endothelial and perithelial cells, as demonstrated by this study.

In agreement with other authorities whom they quote, the authors believe that it is the slumbering perivascular adventitial cells that acquire, by an upset of the equilibrium, either lymphoblastic or myeloblastic tendencies. Attention is called to the striking similarity of myeloid metaplasia of the spleen with Gaucher's disease.

The conclusions deduced from this study are, briefly: that the splenomegaly of Gaucher's disease is essentially a primary, probably congenital, progressive systemic disease of the hematopoietic tissue, characterized by an aleukemic dysmyelosis; that is, an irregular, perverse myeloid metaplasia. The cells arise from the slumbering myelopotent cells of the reticuloendothelial tissue of the hematopoietic organs. These are principally, and at first, the adventitial cells of the blood channels, and the endothelium of the sinuses. Possibly, later the closely related reticulum also takes on a similar activity. Its etiology, still undetermined, the final conclusion advanced however, is that it is a constitutional anomaly, that is, a mutation in the human species.

LOEBER, New Orleans.

THE CONCENTRATION OF THE PLASMA PROTEINS IN NEPHRITIS. G. C. LINDER, C. LUNDSGAARD and D. D. VAN SLYKE, J. Exper. Med. **39**:887, 1924.

The analyses of the proteins were made by the micro Kjeldahl method of Howe in oxalated plasma. The blood was taken from the vein two to three hours after breakfast, the patients having remained in bed. The patients were divided on the basis of the classification of Volhard and Fahr, into nephrosis (five cases), diffuse glomerulonephritis, subdivided into glomerulotubular (nephrotic) type (eleven cases) and vascular interstitial type (three cases), and nephrosclerosis (five cases).

The averages for eight analyses on seven normal persons were: albumin, 4.11 gm., globulin, 2.61 gm., total protein, 6.73 gm. per hundred cubic centimeters of blood and an average albumin to globulin ratio of 1.6.

In nephrosclerosis there was no decrease in the plasma proteins. With heart failure the ratio of albumin to globulin fell to about one.

In glomerulonephritis of the vascularinterstitial type there was no decrease in the plasma proteins until shortly before death.

In the glomerulotubular or nephrotic type, active or recently active, the total plasma proteins were less than 5 gm. per hundred cubic centimeters.

This decrease from the normal occurred whether or not edema was present. The decrease affected chiefly the albumin, the globulin being usually but little diminished and sometimes slightly increased with the result that the ratio of albumin to globulin was reduced to less than 1, and occasionally to 0.6.

In nephrosis similar changes were found in the total protein concentration, but in severe cases the decrease in the albumin was greater than in nephrotic glomerulonephritis and the ratio of albumin to globulin ranged down to 0.26.

With the disappearance of edema there was usually an increase in plasma protein concentration, but this was not invariable, and concentrations of 4.5 per cent. or less were compatible with persistent absence of edema. The ratio of albumin to globulin showed an irregular tendency to rise. Whenever the total concentration was less than 4 per cent. there was some edema present, but it was sometimes slight in amount.

With recovery in acute cases, and remission with decrease of proteinuria in chronic cases, normal concentrations were regained. The albumin: globulin ratio remained low in some instances for a longer period on account of an absolute increase of globulin concentration.

In "functional proteinuria" (two cases) no changes in plasma proteins were found.

Low plasma protein concentrations were always associated with considerable losses of proteins in the urine, but these losses did not provide an explanation for all observations. A disturbance in the production of the plasma proteins appears probable.

CHANGES IN THE VOLUME OF PLASMA AND ABSOLUTE AMOUNT OF PLASMA PROTEINS IN NEPHRITIS. G. C. LINDER, C. LUNDSGAARD, D. D. VAN SLYKE and E. STILLMAN, J. Exper. Med. **39**:921, 1924.

In a preceding paper it was shown that a considerable fall occurred in the concentration of protein in the plasma of patients having nephrosis or glomerulonephritis of the nephrotic type. The question arose whether this abnormality of the plasma proteins was due in any degree to dilution; whether a plasma previously normal in volume and protein concentration became greater in volume and poorer in proteins by retention of extraneous water in the blood.

Using the original vital red method of Keith, Rowntree, and Geraghty and making the measurements about two hours after breakfast which meal contained as little fat as possible, the authors determined the absolute volumes of plasma and blood in a series of nephritic patients with low plasma protein concentration and with all degrees of edema. For purposes of comparison and calculation, they took as the standard body weight, the actual or calculated weight of the patient when edema free.

They did not observe gross increases in plasma volume in glomerulonephritis, nephrosis, or nephrosclerosis, even when the concentration of plasma proteins was much below normal. Their results indicate the probability that "hydremic plethora" does not occur.

The low protein concentration frequently observed in the plasma in nephritis is not due to increased plasma volume, but to a decrease of total amount of plasma protein in the body.

Changes in plasma volume showed no constant relationship to changes in edema.

FAT METABOLISM IN NEPHRITIS. A. HILLER, G. C. LINDER, C. LUNDSGAARD and D. D. VAN SLYKE, J. Exper. Med. **39**:931, 1924.

It is known that in some cases of nephritis there is an increase in the blood lipoids, sometimes to the extent of 100 per cent. or more above normal. In the literature there appear various views as to the reason for this.

The authors attempted to find out whether this increase is due to retarded rate of fat combustion, or to a retardation of its deposition from the blood into the tissues.

The plasma lipoids, the respiratory quotient and total metabolism of nephritic and normal subjects were determined before and after ingestion of fat (butter) in the proportion of 1 gm. per kilogram of body weight.

After fat ingestion a greater increase of fatty acids and lecithin was noted in the plasma of nephritic patients with initially high blood lipoids than in the plasma of normal subjects or of nephritic patients without constant lipemia. In cholesterol no differences were found.

Nephritic patients with constant lipemia were able to burn fat as efficiently as normal persons.

The accumulation of fat in their blood may be due to a disturbance in the mechanism for transferring lipoids from blood to the tissue depots.

McCLURE, Evanston, Ill.

Nervous Diseases

THE ACTION OF CALCIUM CHLORID ON THE VEGETATIVE NERVOUS SYSTEM. L. QUARANTA, Arch. di patol. e clin. med. **3**:57, 1924.

Calcium chlorid was given intravenously to human subjects. The effect of the injection on the reaction of the subject to epinephrin and to pilocarpin was studied. Subjects who reacted strongly to one of these drugs showed less reaction after calcium chlorid had been given, and patients who reacted weakly to these drugs showed a stronger reaction. Therefore, calcium seems to act as a regulator of the vegetative nervous system, and should be useful in patients showing nervous derangement of sympathetic or parasympathetic types.

HIGGINS, Cincinnati.

TETANY AND ALKALOSIS. OTTO TEZNER, Monatschr. f. Kinderh. **28**:97, 1924.

In his review of the subject of tetany in infants with particular reference to the influence of alkalosis, Tezner has attempted to quote every recent article on the subject, and, so far as one can make out, seems to be staggering under his burden. He has attempted some work of his own by producing an alkalosis in dogs by hyperventilation of the lungs and, in other experiments, has determined the effect on electric excitability by feeding sodium bicarbonate.

As regards hyperventilation his problem was to determine whether the tetany resulting was due to a decrease of carbon dioxid as such or due to alkalosis in general. His results show that the respiratory tetany depends on the alkalosis.

The continuous feeding of sodium bicarbonate, leading to a highly alkaline urine causes some increase in electric excitability in some normal children but by no means all. It never elicits a Trousseau sign or convulsions.

The writer maintains, however, that even though alkalosis may increase electric excitability in some cases, it does not follow by necessity that every case of electric excitability and of tetany must be due to alkalosis.

The argument in favor of alkalosis as a cause, namely, the good results following therapy with hydrochloric acid or ammonium chlorid, Tezner meets with the reply, "Because a drug influences a condition, one cannot conclude that the drug had anything to do with the cause. It is possible that alkalies may increase electric excitability, acids diminish it, and still neither have anything to do with the etiology." Tezner concludes his paper by quoting two cases of tetany in infants uninfluenced by ammonium chlorid treatment.

GERSTLEY, Chicago.

OBSERVATION ON THE QUESTION OF THE ETIOLOGY OF SPASMOPHILIA. NICOLAI JOHANNSEN, Acta Pediat. **3**:168 (Feb.) 1924.

Johannsen found that feeding sodium carbonate to children with latent tetany, regularly produced symptoms of active tetany and increased the electrical irritability. In normal children this treatment caused some increase in electrical irritability, but reactions characteristic of tetany were not obtained. He concludes that disturbances of salt metabolism are concerned only in bringing out active symptoms of the disease. The fundamental disorder is something deeper, possibly a deranged parathyroid function. He is inclined to attribute the effect of sodium carbonate to a sodium plus ion intoxication rather than to the alkaline properties of this salt. He admits, however, that this latter may exert some influence, and presents data to show that hydrochloric acid and acid producing salts like ammonium chlorid caused improvement in symptoms and electrical reactions.

He observed a few cases of tetany which did not respond to calcium therapy, and concludes from this that there may be several kinds of tetany.

HOLT, Baltimore.

AN HISTOLOGICAL STUDY OF THE CENTRAL NERVOUS SYSTEM IN EXPERIMENTAL BOTULINUS POISONING. E. V. COWDRY and F. M. NICHOLSON, J. Exper. Med. **39**:827, 1924.

Physiologic experiments by Dickson and Shevky and by Edmunds and Long afford evidence that the peculiar and distressing symptoms of botulinus poisoning may be explained on the hypothesis that the site of action of the toxin is on nerve terminals, and that the paralytic features are not of central origin, as was formerly supposed. This casts suspicion on the older work, largely histologic, tending to show that the toxin acts directly on the central nervous system and particularly on the respiratory center presumably in the medulla.

The authors studied histologically the brain and spinal cord in mice, guinea-pigs and rabbits which had been injected with botulinus toxin and kept until they showed very pronounced symptoms when they were etherized and tissues removed for examination. They state that their observations indicate that, except for a slight degree of vascular engorgement, all the lesions which they noted in the brains of mice, guinea-pigs, and rabbits suffering from botulinus poisoning are readily susceptible of some explanation other than that they are produced by the direct action of the toxin on the central nervous system.

Although absence of microscopic evidence of a central action of the toxin is not conclusive proof that the brain cells are not primarily involved, yet the observations tend to show that, on the histologic side, there is no evidence inconsistent with the results of physiologic experiments, indicating that the site of action of the toxin is on peripheral nerve terminals.

MCCLURE, Evanston, Ill.

Diseases of the Nose and Throat

INDICATIONS FOR TONSILLECTOMY WITH A CRITICISM OF THE OPERATION. GILBERT H. LANSDORON, Canad. M. A. J. **14**:379 (May) 1924.

The indications in children are: (1) interference with respiration, deglutition or voice production; (2) interference with normal passage of air into and from middle ear via eustachian tube either by displacement of palate or direct obstruction; (3) tonsils as foci of infection. Enlargement of cervical glands is an important sign of chronic tonsillar infection.

Complete tonsillectomy is advised. The patient is prepared for operation by giving calcium lactate for three days preceding the operation. General anesthesia is used. The technic of the operation is described in detail.

MOORE, Omaha.

Diseases of the Skin

A Case of Cutis Striata. Urban Hjärne, Acta Pediat. **3**:233 (Feb.) 1924.

The condition described consists in a hypertrophy of the skin of the neck, particularly below the ears which results in the skin being thrown into vertical folds. It is sometimes known as cutis gyrata. Apparently it is a congenital malformation, the development of which is not clear. The author thinks it represents an atavistic tendency, inasmuch as lions, tigers, pumas and other animals normally possess such redundant skin on the neck.

Holt, Baltimore.

Nevi and Their Treatment by Radium. Hugh Mackay, Canad. M. A. J. **14**:394 (May) 1924.

The author advises use of radium for removal of superficial vascular nevi. The capillary nevi are treated by moving a 5 or 10 mg. plaque, the face of which is protected by oiled silk or rubber dam, over the involved area, allowing five minutes for each square represented by size of plaque. Six weeks is the satisfactory interval between treatments.

Deep or cavernous nevi are best treated by implanting two or three steel needles, each containing 12.5 mg. of radium elements, 2 cm. or farther apart in the mass for from three to five hours. In babies an anesthetic is administered for implantation of the needles. The deeply infiltrated port wine nevus is not favorably affected by radium and the prognosis is not good.

The hairy nevi are best removed by excision. The author advises either leaving pigmented nevi alone or else making a wide excision.

Six case histories are reported with photographs.

Moore, Omaha.

Miscellaneous

Light Therapy (Review). Cesare Patrizi, Arch. di patol. e clin. med. **3**:61, 1924.

This article is a review of the whole subject of light therapy. Literature, apparatus and application to different diseases are discussed. There are chapters dealing with natural and artificial heliotherapy, with chromotherapy and with thermotherapy.

Clinical Calorimetry. Carlo Barinetti, Arch. di patol. e clin. med. **3**:195, 1924.

This article is a review of the literature and methods of clinical calorimetry. The different apparatus for determining basal metabolism, especially by indirect calorimetry, are described in brief. The various factors, such as diet and age, affecting the normal basal metabolism, and the influence of pathologic conditions, such as endocrinopathies and fever, on the basal metabolism are discussed.

Higgins, Cincinnati.

Enuresis. Arthur B. Chandler, Canad. M. A. J. **14**:413 (May) 1924.

Various theories and treatment of enuresis are discussed. The author believes that enuresis in the vast majority of cases is due to the failure of development of the higher inhibitory centers through lack of training or injudicious management.

The treatment consists in proper suggestion, training in use of sphincter muscle and establishment or regular habits of urination.

The author believes that drugs, surgical procedures and use of glandular extracts have not given any results in treatment of this condition.

MOORE, Omaha.

NARCOTIC DRUG ADDICTION. II. THE PRESENCE OF TOXIC SUBSTANCES IN THE BLOOD SERUM IN MORPHIN HABITUATION. EMIL J. PELLINI and ARTHUR D. GREENFIELD, Arch. Int. Med. **33**:547 (May) 1924.

This second paper deals with the question of whether any specific toxic substance is produced by morphin habituation. The authors state that since the results of the work of Valenti, who in 1914 reported a series of experiments which tended to answer the question in the affirmative, his results had never been tested by other investigators, and they have therefore made the study of this question the subject of the present paper. Their work consisted of duplication of the most significant feature of Valenti's work and of additional tests of their own, a detailed account of which is given. The authors criticize Valenti's faulty technic and question the methods of arriving at his conclusions, and stress the negative findings of other investigators along similar lines as well as their own, they conclude that (1) no toxic substance is formed in the blood of dogs habituated to morphin which is capable of producing circulatory disturbances in normal animals into which the serum is injected; (2) they find no evidence that any toxic substance is present in the blood as a result of morphin habituation.

LOEBER, New Orleans.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

Thirty-Sixth Annual Meeting, held in Pittsfield, Mass., June 5-7, 1924.
First Session.

DAVID M. COWIE, M.D., *in the Chair*

JUVENILE MEDICINE AND ITS PROBLEMS. Presented by DR. D. M. COWIE, President.

Pediatricians have devoted so much attention to infant feeding, that the field is fairly well covered, and they might better attack the problems of juvenile medication and the diseases of infancy, and of childhood more vigorously. Certain problems require further light, such as the maximum amount of food which may be taken by the growing child without injury, the relations of the pancreas to appetite and metabolism in general, the delayed effects of infections, the effects of local or mild infections on pancreas function, and on kidney function, etc. The family doctor should have better knowledge of juvenile medicine. Certain problems such as the prevention of endemic goiter and mental hygiene, are public health problems which require development by the juvenile internist and then education of physicians, teachers and parents.

How many adult neuropathies and menstrual disturbances, as well as other adult diseases could be prevented by proper attention during the juvenile period? Prevention of infectious diseases by vaccination methods, posture clinics, and behavior clinics should be under the direct supervision of the physician.

The working out of the problems requires a thorough training in adult internal medicine and close cooperation with many specialties, as well as the instruction of medical students, physicians, and the laity.

AN APPRECIATION OF DR. GEORGE N. ACKER was presented by DR. SAMUEL S. ADAMS.

DR. JOHN HOWLAND read a brief account of the medical life of DR. HOLT, and touched on the character of Dr. Holt as a physician, teacher and friend. Dr. Blackader spoke of Dr. Holt's position in the pediatric world and especially the esteem in which he was held in Canada.

REFLECTIONS ON CONGENITAL SYPHILIS. Presented by DR. LEONARD FINDLAY (Glasgow).

DISCUSSION

Paper appears on Page 133.

DR. JEANS: It is indeed a pleasure to hear this subject discussed by one who has given it such careful study. Dr. Findlay's experience has been parallel with ours in St. Louis in many respects. There are, however, a few points that might be discussed on which we have had a slightly different experience. In one chart it was noted that one-third of the children gave positive Wassermann reactions, some gave questionable positive and questionable negative reactions, and some definitely negative reactions. We have not had that experience; for the most part our reactions have been strongly positive or absolutely negative. Only occasionally did we get a doubtful reaction, and on retest they nearly always turned out to be negative. Only to a small extent have we had doubtful reactions in the older children at the end of childhood and at the approach of adult life.

There are a number of points of interest, but they cannot all be discussed in the short time at our disposal. Dr. Findlay mentioned the matter of strains

of spirochetes; from the purely clinical point of view the behavior of the spirochete may be dependent, not on the strain itself, but on its virulence and on the susceptibility of the person infected. For example, take twins, one with central nervous system infection and the other with the nervous system free from involvement. Is there here a definite neurotropic strain or a difference in susceptibility?

Dr. Findlay spoke of the lack of other symptoms when the nervous system was affected. This has been noted in our cases also. Relatively few of our neurosyphilis cases have had interstitial keratitis, though interstitial keratitis affects fully one-third of the older syphilitic children.

With regard to patients who were Wassermann fast and who did not readily give a negative reaction after more or less intensive treatment, it has been our observation that it is these patients who are most likely to have central nervous system involvement. I would like to know if that is the case in Dr. Findlay's material.

Dr. Findlay mentioned the lack of contagion from infants with hereditary syphilis. We have observed no case of contagion from these cases. This is rather surprising because of the great number of spirochetes in cutaneous lesions, for we know that in most cutaneous lesions spirochetes are found in considerable abundance by dark field examination.

DR. HEIMAN: It seems to me that Dr. Findlay in his remarks tried to defend the large amount of syphilis ascribed to Scotland. Of course that would only hold good in cases of syphilis neonatorum in which the Wassermann test has been positive. Syphilis may be of the maternal type or the paternal type or both, and the time of infection of the mother is an important factor. In cases of recent origin the mothers abort and this must be considered congenital syphilis. Those who have an infection of less recent origin miscarry, and again we must consider these as cases of congenital syphilis; then we have the cases in the new-born. We must also take into consideration the fact that some infants born of syphilitic parents may not have demonstrable spirochetes but may be parasyphilitic. A great deal depends on the strains of spirochetes and their virulence and also on the resistance of the patients. We know that certain strains have a predilection for certain tissues, as they have for the nervous system or the viscera. As to the susceptibility, in certain patients only certain organs will be affected.

DR. VEEDER: In regard to the question of treatment. Two or three years ago we checked up 434 cases of congenital syphilis, which had been treated in the clinics connected with Washington University, during the previous five or six year period. We came to the conclusion that treatment as a whole had been unsatisfactory, and that for congenital syphilis the only effective treatment is preventive. While a certain percentage of clinical and Wassermann cures had been obtained, a large part of the treatment had been ineffective, and if the economic side of treatment is considered the results were most disappointing. We came to the conclusion that emphasis should be put on the angle of prevention. We have been testing all mothers in our prenatal clinics, and putting all those with a positive Wassermann reaction on antisyphilitic treatment. In this way we have obtained the same results as others have before us, in minimizing the number of infants born with congenital syphilis. This work, however, constitutes a community problem rather than a problem of the individual patient, and I believe that by working on the subject from that standpoint it will be possible to eliminate the majority of cases of congenital syphilis.

DR. FREEMAN: Dr. Findlay spoke of the accuracy of clinical diagnosis. I should like to ask him of what significance he considers the so-called syphilitic wig. We have had a number of these cases and in all of them the Wassermann reaction proved to be negative.

DR. FINDLAY (in closing): The point I have wished to emphasize is that the incidence of congenital syphilis has been greatly exaggerated. While the

Wassermann test is a very reliable means of detecting the presence of congenital syphilis, we must remember that a positive reaction in the new-born is not always proof that the child is syphilitic, since although the antibodies may pass over from the mother to the child the spirochetes may not enter the circulation of the infant.

As to the so-called "syphilitic wig," I would not regard it as evidence of syphilis.

In a great many cases the difference in diagnosis is due to the weight placed on the value of the Wassermann reaction. I think perhaps that accounts for the difference between Dr. Jeans' results and ours; perhaps Dr. Jeans has laid more stress on the value of the Wassermann reaction in the new-born than we have done. Dr. Jeans, judging from his recent work, has tried out the Wassermann reaction in a number of patients, and finding it positive has concluded that these are cases of syphilis.

In regard to neurosyphilis, unfortunately, in a series of cases of clinical neurosyphilis one first discovers the condition when there are nervous symptoms, such as spastic paralysis, tabes, etc., and then examination of the cerebrospinal fluid will give a positive Wassermann reaction. I think that if Dr. Jeans had worked on the same basis as we have done his results would not differ greatly from ours.

The Wassermann reaction we have found to vary, and we have found a certain proportion of doubtful reactions; we have not had Dr. Jeans' experience of sharply negative and sharply positive reactions. In our spinal fluid examinations we have had doubtful reactions, but we have included all those as positive which could with any justification be so classed.

As to the question of the contagiousness of congenital syphilis, the lack of contagion is very striking when one considers the way in which children are embraced and kissed and how seldom the disease is communicated. I have seen one example of contagion. A grandmother was infected by her grandchild, but cases of this kind are rare.

I do not think I have anything more to add except to say that I am very pleased to hear that Dr. Veeder agrees that the solution of the question of congenital syphilis lies in prophylaxis and not in the attempt to cure actual cases of the disease.

HYPOGLYCEMIA AND ACIDOSIS. Presented by DR. FRITZ B. TALBOT, DR. EDWARD B. SHAW (by invitation) and MISS MARGARET E. MORIARTY, S.B. (by invitation).

Howland and Marriott drew attention to the fact that in severe acidosis the alkali reserve of the body was greatly lowered. Gamble and other investigators later showed that during fasting the alkali reserve was lowered "in consequence of the unusually large concentration of organic acids in the blood plasma."

Our studies indicate that the great production of ketones is dependent on a diminution of the available sugar in the child's body. This is illustrated by three children who underwent voluntary fasts for its therapeutic effect on idiopathic epilepsy.

Charts are shown in which the blood sugar reached an average of 45 mg. per hundred cubic centimeters of blood and in one instance, 38 mg. With the exception of the latter case, symptoms of hypoglycemia were not evident. The younger the child the more rapidly the glycogen reserve of the body is apparently depleted, as hypoglycemia is not found in the fasting adult.

Although the data presented in the foregoing are incomplete and are given as a preliminary report of investigations that are now in progress, they form the basis on which to build up the probable sequence of events which is briefly outlined here. During health, the heat energy of the body is derived principally from the combustions of carbohydrate, and to a lesser degree from fat and protein. Under these conditions there is, of course, a great excess of antiketogenic

material. During a fast, however, as no carbohydrate is obtained from food, the store of available carbohydrate in the body is quickly exhausted. Confirmatory evidence of this is found in the low blood sugar concentration before mentioned. The heat energy then must come from fat, and to a much less extent from protein. The balance is now thrown in the other direction, and there is a great excess of ketogenic material which is not entirely compensated by the small amount of carbohydrate obtainable from the protein. There is, in consequence, a great production of ketones. The ketone acids then combine with the alkali of the blood and reduce the carbon dioxid combining power. This decrease in the alkali reserve is accompanied in our cases by a diminished alkalinity of the blood as shown by the p_H. If this sequence of events is correct, then acidosis during fasting with nondiabetic children is due to a lack of available sugar which is manifested by a low blood sugar content.

The material reported was obtained during voluntary fasts, although the same conditions are present in involuntary fasts, such as are occasionally seen in prolonged vomiting, in cyclic vomiting, and at the onset of some of the acute infectious diseases and after etherization. We believe that sufficient data are now available to state that one type of acidosis, that associated with starvation, is due to a deficit of available sugar in the blood.

DISCUSSION

DR. GAMBLE: Dr. Talbot's charts illustrate a point which the recently devised colorimetric method for determining plasma p_H has taught us, namely, that lowering of the plasma bicarbonate is accomplished by a considerable fall in p_H, i. e., an increased plasma acidity. Because of the theoretical possibility of compensation for a lowered bicarbonate by a proportional lowering of the free carbonic acid in the plasma through respiratory adjustment, we have been inclined to believe that little actual increase in plasma acidity took place even in the presence of a greatly reduced bicarbonate. Direct measurements of plasma acidity by Cullen's method have shown us, however, as illustrated by Dr. Talbot's charts, that even moderate reduction of bicarbonate causes a considerable fall in p_H. In other words, compensation is not nearly so complete as has been supposed, and a lowering of the plasma bicarbonate may then be taken as dependably indicating an appreciable increase in plasma acidity.

DR. GERSTENBERGER: It seems to me that Dr. Talbot's paper is of decided practical importance, especially to the general practitioner. I have found that many men in practice are mainly concerned in insuring an increased intake of protein during and following starvation due to sickness and vomiting, and as a result are usually prescribing proteins in concentrated and predigested forms.

It has been our practice for some time to teach medical students that an adequate carbohydrate intake is of greater and more immediate importance in these cases than is a high protein intake. A malt soup which is low in protein and fat and high in calories is a type of carbohydrate that is our choice, especially for the older children.

DR. SCHLOSS: The extremely low blood sugar values which Dr. Talbot has found in starvation are quite comparable to blood sugar values obtained by Dr. Weymuller under somewhat different conditions. Dr. Weymuller's observations concerned feeding children high ketogenic-antiketogenic ratios. When severe ketosis developed he found blood sugar values quite comparable to those of Dr. Talbot. Further observations by Dr. Weymuller on fasting children, who were subject to spontaneous ketosis, also are of interest in comparison with Dr. Talbot's results. These children also developed very low blood sugar during a fast, the values of 40 mg. per hundred cubic centimeters being obtained in several instances. These low blood sugar values, however

in children subject to ketosis appeared on the second day of the fast, which is in marked contrast to the results obtained by Dr. Talbot on normal children showing the occurrence of low blood sugars after the fourth day. This is quite in keeping with other evidence which we have obtained, which would seem to show that ability to store glycogen is reduced in children subject to ketosis. A question somewhat aside from the main issue of the discussion but of the greatest interest, is the cause of the symptoms in clinical ketosis. The amount of acetone in the blood in comparison with the results of animal experiments is totally insufficient to exert a profound anesthetic effect. It is possible that the acidosis may be responsible for part of the symptoms, as it is well known that the injection of mineral acids into animals may produce coma or pronounced nervous symptoms. On the other hand, Barr and his co-workers have found that following muscular exertion a considerable degree of acidosis may occur without any disturbance of the sensorium and without profound discomfort.

DR. HOWLAND: Dr. Talbot and Dr. Gamble have shown that when children with epilepsy are deprived of food they react rather regularly with a lowering of the bicarbonate of the plasma, a diminution of the blood sugar and an increase of ketone bodies in the urine. These changes reach their maximum on the third or fourth day, and thereafter there is a gradual shift toward normal values. In this connection some observations made by Dr. Ross and Dr. Josephs are of interest. They made observations on a boy who would develop convulsions with each febrile disease from which he suffered if he refused to take food. His blood sugar would fall to 40 mg. per hundred cubic centimeters and he would develop a considerable degree of ketosis. When glucose was administered the symptoms disappeared rapidly. He never had convulsions except when wasting. The boy was seen in several attacks. It was found that when he was purposely deprived o fo od the blood sugar fell, and ketosis developed much more rapidly than with other supposedly normal children. A striking change was observed in only twelve or sixteen hours instead of in three or four days. It appears that there are some children who react more rapidly and sharply than others, and this may be an explanation for the occurrence of certain of the attacks of recurrent vomiting. If one studies the histories of a large series of cases of recurrent vomiting it will be found that convulsions occasionally occur without apparent cause. The thought at once arises that these convulsions may be due to the same cause that produces them with an excessive dose of insulin, i. e., hypoglycemia. These children perhaps may not store or mobilize glycogen so readily as normal children and this may account for the rapid lowering of the blood sugar.

DR. CHARLES HENDEE SMITH: The nervous reaction of the individual child plays a part in many of these cases of ketosis with vomiting. For several years I have used bromids by rectum in addition to glucose, and have secured control of the symptoms much more quickly than with carbohydrate alone. By administering bromid in this way it is possible to cut down the duration of vomiting from the usual period of from three to five days to twelve hours in many instances.

DR. COWIE: A few years ago (1921) Parsons, Greenthal, Hoag and myself made some investigations of this kind. We took normal children, starved them for a few days and estimated the carbon dioxid combining power of the blood, carbon dioxid alveolar air, breath and urine acetone, blood sugar, total non-protein nitrogen, blood fat and the ordinary urine chemistry. In one case the carbon dioxid combining power of the blood went below twenty. Dr. Hoag, who worked with me at that time is here. May I ask him if he recalls the figure?

DR. HOAG: As I recall it, it was not so low as 20. I think about 24 was the lowest [Reference to the observations shows that the lowest carbon dioxid was 21.1 by the Van Slyke method. D.M.C.].

DR. COWIE: At any rate we were inclined to think the carbon dioxid was getting pretty low. I think we did not carry our starvation period quite so long as Dr. Talbot has done without the addition of some food. The blood sugar characteristically dropped. We did not follow the hydrogen-ion concentration of the blood as Dr. Talbot has. Previous to this work we had been using glucose intravenously and by rectum in cases of cyclic vomiting, with a view to overcoming the developing acidosis. Our observations verify the work of Dr. Talbot. They have not been published.

DR. TALBOT (in closing): One point which I did not bring out and which I should have mentioned is the fact that in all these cases we had a measured fluid intake of 60 ounces (1,774 cm.) a day. Two children in the series took less than this amount and complained of marked discomfort. These symptoms disappeared after the fluid intake was increased. So long as the children took large amounts of fluid they had no symptoms of acidosis. The point that I would like to emphasize particularly is the lowering of the blood sugar. As we were studying other conditions it was borne in on us more and more that the glycogen reserve of the body from the clinical point of view is the factor that is going to assume considerable importance, and it must be considered in the clinical treatment of cases. I do not believe there are many men here who have patients operated on for tonsils or adenoids or other conditions requiring surgery without preparing them for operation, by taking the precaution of administering glucose and as much fluid as possible. This may explain the better results in postoperative treatment than were obtained before the ketogenic balance was taken into consideration.

It was suggested that the carbon dioxid combining power of the blood struck a level and did not fall any further. That was true of the fasts that we observed, but I think that if the fast had been carried on beyond the point where there was available carbohydrate from protein sources that we might have had acidosis that was dangerous.

POSTOPERATIVE ACIDOSIS IN CHILDREN. Presented by DRS. PHILLIP C. JEANS and KENNETH H. TALLERMAN (by invitation).

A study has been made of children with a view to elucidating the causation of postoperative acidosis. The blood and urine before and subsequent to operation were followed, and those substances which might be causative factors were estimated. The data presented demonstrate that the lowering of the alkali reserve is due in but small measure to acetone bodies, or to lactic acid accumulation. Phosphorus retention is obviously not the cause of any acidosis that may exist. In fact phosphate retention constitutes a compensatory mechanism, the phosphates of the blood falling with a lowered alkaline reserve, and the phosphorus excretion being increased coincidently. The organic acids excreted increase, and in those instances showing a more marked lowering of the blood carbon dioxid, are in excess of both acetone bodies and lactic acid. It is therefore presumed that some as yet unidentified factor is largely responsible for the lowered alkali reserve which is observed. The fall of the carbon dioxid appears proportional to the drop in blood pressure. It was observed also that qualitative tests for acetone bodies in the urine gave but a poor indication of the degree of acidosis present, if compared to the variation in the alkali reserve.

DR. SCHLOSS: Dr. Jean's results are extremely interesting. There has been considerable discussion concerning the cause of the lowered plasma bicarbonate after anesthesia. I am particularly interested in the disparity he has found between the ketone acids and the total organic acids. Dr. Weymuller, in investigations to be published shortly, has found the same lack of correspondence in acidosis due to starvation, and also due to feeding infants a larger amount of fat than the ingested carbohydrate can take care of. This lack of correspondence was particularly marked in children who were fed on a ratio of from

two to three parts of fatty acid to one of glucose, according to Woodyatt's calculations. This unexplained organic acid fraction appears, therefore, under the same conditions that the ketone bodies appear, and in our experience, disappear very rapidly after the administration of glucose. I have no suggestion beyond this as to their origin or nature.

DR. BLACKFAN: Drs. Talbot and Jeans have indicated the reason for the excellent results from the administration of glucose in infants and children who, as a result of infection, show grave manifestations of acidosis. Mention has been made of giving water by injection. We refer to the use of glucose very frequently in the treatment of this condition, but I do not believe that enough emphasis is placed on the need for a great deal of water in children suffering from acidosis. I have been interested for some time in the manner in which water should be introduced. I feel that if water is given orally in relatively large quantities, the small child cannot obtain a sufficient amount of water quickly enough to influence the condition favorably. Therefore, I believe water should be introduced parenterally, intravenously or intraperitoneally. The introduction of physiologic sodium chlorid solution subcutaneously followed by the intravenous injection of hypertonic glucose solutions results in the very rapid absorption of water. Water should be given in large amounts, so that it can be absorbed as rapidly as possible in order to overcome the effects of the unknown acids which play an important part in the production of acidosis.

DR. GAMBLE: Dr. Jeans' finding depends chiefly on the very ingenious method of Van Slyke and Palmer for measuring by direct titration the total organic acid excretion. There are at least two conditions in the urine which will cause an enormously large measurement by that method, the presence of albumin or of bicarbonate. As regards bicarbonate, we have found that it is not dependably removed by the calcium hydroxid, which is meant to precipitate the phosphates and carbonates. Urine of usual acidity, however, does not contain an appreciable amount of bicarbonate. Error due to it would be encountered only in urines more alkaline than p_H 7.0. I would not guess that either of these causes of error were present in Dr. Jeans' material. I wish to draw your attention to them simply because this organic acid method is not much used in studies of acid excretion under various circumstances.

DR. JEANS (in closing): With reference to what Dr. Gamble has said, none of these urines contained albumin and all were tested with cresol purple; but one or two of the urines were neutral, while most of them were acid.

SOME FURTHER OBSERVATIONS ON THE LANGE GOLD CHLORID REACTION ON THE CEREBROSPINAL FLUIDS IN INFANTS AND YOUNG CHILDREN. Presented by DR. GRULEE.

Paper appears on Page 147.

DISCUSSION

DR. JEANS: Formerly we used the colloidal gold reaction to a considerable extent, not only in relation to the diagnosis of syphilis but in relation to a number of central nervous system lesions; we came to the conclusion that its field of usefulness is rather limited. It seemed to serve in some instances to distinguish between the paretic type of lesions and the meningitic type, but Dr. Grulee has even discredited its usefulness for this purpose by showing two cases in which the results were not in conformity with the actual findings. He has shown that there were moderate reactions when no changes were detected, so far as other methods could determine. He also found reactions in cerebrospinal fluid from cases of epilepsy, when by any other method no change in the cerebrospinal fluid was found. It seems to me the field of usefulness of the colloidal gold reaction is extremely limited. It is more of academic interest than of real practical value.

AMERICAN PEDIATRIC SOCIETY

Second Session

CLINICAL STUDIES OF SOME DISEASES OF THE BLOOD IN CHILDREN, WITH ILLUSTRATIVE CASES. Presented by DR. J. P. CROZER GRIFFITH.

The more recent knowledge of the physiology and pathology of the blood was intentionally not discussed, and full admission was made that the usual clinical methods for the determination of the percentage of hemoglobin suffer from inaccuracy. Yet for ordinary bedside studies of the blood the methods hitherto in vogue must be depended on; and they at least answer well for comparison of conditions in adult life and in childhood respectively. Reports of cases were presented illustrating certain features of diseases of the blood in infancy and childhood. A number of conclusions seemed justified.

1. That as much as the ultimate diagnosis of chlorosis rests always on the characteristic condition of the blood, cases in infancy and childhood which present this peculiar relationship of the erythrocytes to the hemoglobin should be called chlorosis, contrary to the statement in many textbooks that the disease is not seen until puberty or later. A number of illustrative cases were reported, one with 5,050,000 erythrocytes and 38 per cent. of hemoglobin. Such cases are frequently encountered at this time of life.

2. That this form of anemia is particularly susceptible to a rapid improvement in the hemoglobin content under simply the administration of iron and without any change in the hygiene or the diet. This improvement is as rapid and as striking as in the chlorosis of adults. This is directly opposed to the statement made in some quarters that iron is of little or no value in the treatment of anemia. The results would seem to depend on the nature of the anemia. Even many cases of the usual secondary anemia, with the percentages of both erythrocytes and hemoglobin much lowered, are distinctly aided by medication with iron.

3. That there is an entire lack of correlation between the degree of anemia and of enlargement of the spleen. A number of cases were reported to illustrate this fact.

4. That there is a remarkable tendency to variation in the blood picture in many cases of diseases of the blood in early life, and cases may show features of more than one blood disorder, or a change from one blood picture to another. Cases were reported exhibiting features suggesting both pernicious anemia and leukemia; leukemia and pseudoleukemic anemia; Hodgkin's disease and leukemia, etc.

5. That the atypical forms of leukemia in early life are more common than the typical, and perhaps especially frequent is the occurrence of lymphocytic leukemia with a total leukocyte count not increased above normal, or even below it. Details were given of a number of cases illustrating this statement.

6. That an excessive number of myelocytes cannot be looked on as positive proof of the existence of leukemia. In one illustrative case there was a sudden temporary rise to 40 per cent. of these cells, and the laboratory diagnosis of leukemia was made; later to be changed to von Jaksch's disease. On the other hand, another case was supposed to be pernicious anemia, in spite of a temporary existence on one examination of 40 per cent. of myelocytes; the diagnosis being altered to myelocytic leukemia some months later when the high percentage of these cells had become permanent.

7. That both prolonged bleeding time and prolonged coagulation time can be present in some forms of purpura in childhood, and that consequently prolonged coagulation time cannot be looked on as positive diagnostic evidence of the existence of hemophilia. The case in a girl, aged 12 years, illustrated this fact.

8. That a single examination of the blood may not be sufficient to establish a diagnosis, often repeated examinations being required; and that there is no one hematologic feature which can be called conclusive.

DISCUSSION

DR. ALFRED F. HESS: I just wish to say a word about this last case, the hemorrhagic case which Dr. Griffith has described. In the differential diagnosis between hemophilia and purpura the main distinctions are the coagulation time, the platelets and the capillary resistance test. This test is made by applying a tourniquet to the arm, which in purpura leads to the production of many hemorrhagic spots on the forearm, while in hemophilia this procedure produces no effect whatever. In purpura there are platelet changes, whereas this sign is negative in hemophilia and the coagulation time is prolonged. There may be variations from this rule and some of the signs may not be definite.

What method did you use for determining the coagulation time?

DR. GRIFFITH: I cannot say what method was used.

DR. HESS: Probably Howell's. By this method the normal coagulation time is from six to ten minutes; in purpura it may be as high as twenty minutes. In true hemophilia there will be a rise to thirty minutes, one hour or an hour and a half. There are exceptional cases. In two instances I have seen irregularities occur in a family of hemophiliacs. The women in families of hemophiliacs may not be entirely free from the condition. I have seen a cousin, and once a sister who had minor symptoms of purpura combined with a coagulation time which was somewhat prolonged.

DR. BARTLETT: I spoke to Dr. Griffith in reference to an interesting case which we have had at the hospital, which fits in with Dr. Griffith's case of leukemia. This baby, aged 14 months, until three weeks before admission to the hospital seemed to be perfectly well. Three days before admission the child began to fail rapidly. The blood examinations while it was in the hospital were as follows:

Date, 1924	Red Blood Cells	Hemoglobin, per Cent.	White Blood Cells	Polymorphonuclears, per Cent.	Small Lymphocytes	Large Lymphocytes	Myelocytes	Transitionals	Basophils	Nucleated Red Blood Cells
March 18	824,000	20	57,100	5	39	55	5	..	2	6
March 19	2,192,000	55	10,000	6	48	45	..	..	1	15
March 21	2,248,000	45	8,500	10	70	13	5	..	1	4
March 24	2,216,000	40	4,950	18	54	20	7	..	..	3
March 26	1,712,000	38	3,700	21	61	11	5	2	..	..
March 29	1,568,000	35	3,050	13	65	14	5	3	..	11
March 31	2,224,000	55	2,600	19	64	5	8	4	..	..
April 3	2,176,000	45	2,050	28	62	8	2	..	..	..
April 5	2,480,000	55	2,250	33	56	5	5	..	1	..
April 9	2,712,000	50	2,350	56	38	4	2	..	..	..
April 17	3,184,000	70	8,250	42	32	22	3	1	4	..
April 25	2,432,000	60	4,400	16	66	12	7	..	..	10
May 5 p.m.	.....	.....	21,150							

At the time of the first count there were acromasia and anisocytosis, 152,000 blood platelets; at the time of the second count there were also acromasia and anisocytosis. On April 3 there were 1 myelocyte and 80,000 blood platelets. At the examination on March 21, there were nucleated red cells and stippling.

The child died, May 5, when the leukocyte count was 21,150. The liver and spleen were enlarged. The spleen increased in size while the baby was under observation. A complete necropsy was performed. The surface of the liver gave the appearance of polished marble, very thin, through which one could see myriads of lymphatic deposits. There were petechial spots on the back of the legs.

The case illustrates the low leukocyte counts not infrequently seen in acute lymphatic leukemia.

DR. GRIFFITH (in closing): Nothing which I said was intended to indicate that the last case reported was one of hemophilia. That was not the diagnosis. The case illustrates only that more or less prolonged coagulation time may

exist in purpura, although not to the degree seen in hemophilia. The method employed was one which did not exclude the presence of the tissue juices. If these had been excluded the coagulation time would probably have been still more prolonged.

Dr. Bartlett has shown what I wanted to bring out, namely, that there is no one sign on which we can base a diagnosis in the anemias of infancy and childhood. They present such a kaleidoscopic picture, such changes in the blood picture from one time to another, that it may be very difficult to make a diagnosis. To obtain the differential count is an absolute necessity, and even a single count often leaves one in doubt if dependence is placed on that alone.

An interesting article by Garrod, Thursfield and Taylor appeared in the British Journal of Children's Diseases, in which the authors, with illustrative cases, point out many of the features on which I have been dwelling; especially that the leukemias of childhood and infancy are more often atypical than typical, and that there is no rule at all regarding the increase of white corpuscles in the blood.

THE CLINICAL VALUE OF THE ROUTINE EXAMINATION OF BLOOD SMEARS IN THE DIAGNOSIS OF PERTUSSIS: A REPORT OF 300 CASES. Presented by DR. HENRY HEIMAN.

The routine examinations of blood smears in all cases of pertussis suspects is especially important because there are no other methods for the diagnosis or control of this disease which have proved of value. The author does not feel that pertussis vaccines or the intracutaneous reactions for testing immunity have been successful.

A review of the literature was presented beginning with the first description of characteristic blood pictures by Fröhlich of Breslau, in 1897.

In the study of 300 cases of whooping cough or whooping cough suspects the author's aim was to perform the simplest, most rapid blood examination in order to make it a more general routine procedure in private practice. The test was based only on a relative lymphocytosis. No total counts were done. One hundred white cells were counted in the usual blood smear, stained with Jenner's dye, and a simple division including only polymorphonuclear cells and lymphocytes was made. The eosinophilic leukocytes were included with the polymorphonuclear and the transitional cells in the lymphocyte counts. Small and large lymphocytes were grouped together. The entire procedure takes but a very few minutes, and can be performed in the course of routine office examinations on all suspicious cases.

The 300 cases were divided into four groups.

1. Clinically positive cases, 124, of which 106, or 85 per cent. showed a very definite lymphocytosis.

2. Suspicious cases which later proved to be positive pertussis, eighty-four. Of these sixty-nine, or 82 per cent. showed a very definite lymphocytosis.

3. Suspicious cases which subsequently proved not to be positive pertussis, fifty-seven. Of these, only ten, or 17 per cent. showed a definite lymphocytosis.

4. Suspicious cases whose progress could not be definitely followed up, thirty-five.

The suspicious cases were all seen within the first two weeks after the onset of the symptoms.

The results of the examination of blood smears in 300 cases of pertussis have been presented, not to demonstrate any new and positive method for diagnosis, but to emphasize the almost constant occurrence of lymphocytosis as a very useful aid in the early detection of this serious infection of childhood.

DISCUSSION

DR. HERRMAN: It certainly is important to be able to make a diagnosis of whooping cough very early, and that statement holds good especially if newborn or very young infants are exposed to the infection. As Dr. Heiman has

so emphatically demonstrated, the other methods of diagnosis can hardly be carried out in private practice or in clinics. The bacteriologic test is good, but it is not easy to make, and the complement fixation test is not a simple procedure, so a simple test that can be carried out in the outpatient department or a physician's office is needed. Other diseases, associated with a spasmodic cough, such as influenza, do not show the leukocytosis or the relative lymphocytosis found in pertussis. Taking the matter all together, if a young infant is exposed to the disease, the case should be treated as one of whooping cough. I have seen two deaths in the new-born as the result of infection from the nursing mother, who was in turn infected by one of her other children. Suspicious cases should be considered as true cases and should be isolated completely.

DR. FREEMAN: I have been using this test for years, but I think a negative leukocytosis early in the disease does not mean that the disease is not whooping cough. I have had cases not give a leukocytosis early in the disease and later when the patients developed a paroxysmal cough leukocytosis was found to be present. If in the paroxysmal stage, whooping cough patients usually give this reaction. I had a child come to me with a diagnosis of whooping cough with a peculiar type of paroxysms that ended in a series of sneezes. There was no leukocytosis. I felt sure it was not whooping cough. My surmise was correct. The condition proved to be wrongly diagnosed, and the paroxysms disappeared when the postnasal irritation was removed by treatment.

DR. COWIE: We have used the differential blood count in my clinic as a test for whooping cough for a long time and place great value in it. We do not depend on a single differential count. If we find a child with a cough and suspect whooping cough, differential counts are made from day to day. The value of the test lies in its aid in the control of whooping cough in the wards. For example, if the entrance history records that the patient has just recovered from whooping cough, a differential blood count is made. If a definite lymphocytosis is found the patient is not admitted until the blood count returns to normal. We feel that this has been a help in preventing contagion in the wards. In very young children one must remember that the blood is likely to revert to the infantile or embryonal type. I think it is often difficult to evaluate the lymphocyte count under these conditions.

DR. HEIMAN (in closing): In regard to Dr. Herrman's expression of opinion that it is difficult to differentiate cases of whooping cough from pseudopertussis. Under pseudopertussis we refer to the influenzal cough, where we have a tenacious mucus which may cause a cough somewhat resembling the paroxysmal cough of pertussis. In cases of this type we do not rely on one count but have the child come back in a week, and that tells us whether they have true or pseudopertussis. That also answers Dr. Freeman's question.

As to Dr. Talbot's borderline case, the only thing to do is to make a subsequent examination. In very young infants with pertussis aged from 3 weeks to 3 months, we have had the lymphocytes run up to 97 or 98 per cent. I have only presented this study because the test is simple and of value. Every one knows that we have a leukocytosis and a lymphocytosis, but I wish to emphasize that we should all attempt to make these examinations in our offices, and that they can be made in a simple way in a few minutes' time.

FUNCTIONAL DIASTOLIC MURMURS IN THE AORTIC AREA, AND PISTOL SHOT SOUNDS IN THE GROINS IN INFANCY AND CHILDBIRTH. Presented by DR. JOHN LOVETT MORSE.

This functional murmur, which is heard rather frequently in association with severe anemias in infancy and early childhood, is audible not only in the aortic area, but is transmitted in the same way as the murmur of organic aortic insufficiency. It may or may not be associated with enlargement of the heart.

If the anemia is marked, it is likely to be accompanied by a Corrigan pulse, with high pulse pressure and a double murmur in the groins. It must be inorganic, because it diminishes and finally disappears with improvement in and recovery from the anemia. It is not probable that the murmur is due directly to the anemia, i. e., to some change in the blood itself. It is presumably simply one of the manifestations of the lowered muscular and nervous tone, produced by the anemia and due to a relative insufficiency of the aorta from dilatation.

A pistol shot sound in the groin is relatively common in moderate and severe cases of anemia in early life, being more common in infancy than later. It is usually associated with an increase in the pulse pressure and occasionally with a double murmur, Duroziez's sign. These manifestations are not evidences of a lesion at the aortic orifice, although they are sometimes accompanied by a diastolic murmur in the aortic area. Proof of this statement lies in the fact that they vary with the intensity of the anemia and disappear entirely when the anemia is cured. They are presumably due to lowered vasomotor tone, which is in turn caused by the anemia; they are not infrequently heard in other conditions in childhood which are accompanied by lowered vasomotor tone, such as pneumonia and typhoid fever. The only importance of these physical signs is that they are sometimes thought to be evidences of organic disease at the aortic orifice and, consequently, the cause of mistakes in both diagnosis and prognosis.

DISCUSSION

DR. GRULEE: There is one point that may be made. There is a certain type of anemia which is likely to be accompanied by many of these phenomena, commonly called aplastic anemia. That type of anemia is accompanied by fever. It might be wise in cases in which the anemia is still advancing and there is no remission in the fever, to take a blood culture. In my experience, in the cases of aplastic anemia this has always been negative, thus providing a differential point from endocarditis.

THE EFFECT OF PREGNANCY ON THE COURSE OF SCURVY IN GUINEA-PIGS. Presented by DR. GERSTENBERGER. Paper appears on page 173.

DISCUSSION

DR. ALFRED F. HESS: This is a very interesting observation of Dr. Gerstenberger. Of course it is just the opposite of what would be anticipated. The dose 5 c.c. of orange juice is a little higher than is necessary. I worked with guinea-pigs weighing an average of 250 gm. and a minimal dose of 1.5 c.c. was satisfactory. It would not be much more for these larger pigs because they were growing less rapidly. The only extensive work of this nature is that of Ingier *Frankfurter Zeitschrift fuer Pathologie,* and in the *Journal of Experimental Medicine.* The experiments gave the same results; many of the pregnant pigs aborted and many fetuses were born dead and those born alive had subacute scurvy. When these were put on a scorbutic diet they very soon developed scurvy. I do not remember what the effect on the mothers was.

In this connection we might learn something from Russia where scurvy is endemic. In looking over the literature I should think there would be something on the different reaction of pregnant and nonpregnant women. I think, as Dr. Gerstenberger has suggested, that many of the signs that we have been accustomed to look for in scurvy such as hemorrhages, are not signs of scorbutus but are the result of the complications of scurvy due to bacteria or to their toxins. Scurvy is a disease that gives few symptoms; it is the complications rather than the disease itself which enables the physician to make the diagnosis.

ST. LOUIS PEDIATRIC SOCIETY

June 5, 1924

GEORGE M. TUTTLE, M.D., *President*

A CASE OF DERMATITIS GANGRENOSA INFANTUM. Presented by DR. H. V. DWYER and DR. G. H. KLINKERFUSS (by invitation).

A boy, aged 14 months, colored, malnourished, convalescing from measles, entered the hospital with bronchopneumonia, rickets and sores about the face and arms. These skin lesions formed as papules, progressed through vesicular and pustular stages, then broke down and formed round, crater-like deeply excavated, gangrenous ulcers, with undermined edges and necrotic bases with seropurulent discharge. Tuberculosis, syphilis and noma were ruled out. Laboratory findings were negative. The lesions continued to progress in spite of local and general treatment. A diagnosis of dermatitis gangrenosa infantum was made and a 1 per cent. solution of resorcinol in saturated aqueous solution of boric acid followed by a dusting powder of thymol iodid were applied. The lesions showed immediate improvement. Three weeks later the child developed chickenpox, the lesions of which, instead of resolving, showed a tendency to necrosis and ulceration similar to the primary condition.

A SURVEY OF THE CONTRIBUTING FACTORS OF ENURESIS. Presented by DR. ADRIEN BLEYER.

Because of lack of a definite pathology, various factors have been mentioned from time to time as bearing on, if not in themselves producing, enuresis, and quite a number of these are commonly discussed with a certain affirmation which makes them acceptable to the reader.

An inquiry into the rôle of some of these factors was made. A group of 250 cases was studied. One hundred and twenty-nine were boys and 123 were girls, showing equal distribution in the two sexes and thus arguing against causes residing in the external genitalia of either sex or diseases especially common to either, as, for example, the prepuce in the male, or pyelitis in the female. Enuresis usually subsides with puberty, earlier in girls than in boys. Study of puerile bladder opposed to mature bladder is thus indicated. Eighty per cent. of cases continued from infancy, 20 per cent. starting later on after some infectious disease or injury. Two were initiated by circumcision, 14 different diseases were mentioned by parents as having caused the trouble.

The idea that enuresis is nothing other than deferred sphincter control is not borne out in this study. Types of the disease, nocturnal and diurnal enuresis, are so definitely different in character that it is surprising rather than to be expected, to find them both present in the same child at the same time.

Malnutrition was not a factor. Charts of the weights and heights of the boys and girls separately showed a slight, but consistent, superiority in these groups over the average.

Twenty-five per cent. of the children were judged mentally deficient, or neurotic, but the fact that 75 per cent. were entirely normal would indicate that the psychic factor is relatively unimportant.

Enlarged tonsils and adenoids were present in 116 children, and of these forty-nine underwent operation. In forty-eight of these there was no favorable effect. One patient was worse after operation.

Eye strain was present in thirty-eight cases, but treatment of the eyes failed to benefit the enuresis.

Circumcision. Thirty-three of the patients had been circumcized, showing the prevalence of enuresis among the circumcized as well as the uncircumcized. In fourteen, operation was performed for the relief of enuresis, with cure in one. In two, circumcision was said to have been a causative factor. Retraction of prepuce in ninety-six boys was without effect.

Small meatus was treated in eighteen cases without benefit. Vaginitis in eight cases showed no relation to the disease. Pyelitis: twenty-two cases. Cure of pyelitis in four cases was followed by cure of enuresis. No such effect on the remaining eighteen, and pyelitis continued in several after cure of the enuresis. Defective posture with albuminuria was found to have no causative relationship to enuresis.

From these considerations it would seem that the usual so-called contributing factors are indefinite. Consequently, the suspicion is strongly aroused that there exists some derangement in the bladder itself, anatomic or physiologic, on which the disease in its true form depends.

A Case of Erythroedema Complicated by Noma. Presented by Dr. John Zahorsky.

V. A., a girl, aged 19 months, was nursed for fifteen months. She had no acute illness during the nursing period. The mother ate a rather restricted diet of meat, potatoes and vegetables. She did not eat much bread. She drank three cups of coffee daily.

The baby was then fed a mixed diet but drank no milk. She ate only white bread, no oats nor cornmeal.

For six weeks the baby was very fretful, did not sleep well, was unhappy and did not play. She kept her fingers in her mouth and suffered from excessive salivation. Her appetite was poor, she lost in weight and was poorly nourished. She rubbed her hands and feet as if they itched. There was no cough, no vomiting or no diarrhea. She could stand and walk but preferred to be carried about. She also lost one tooth.

There was an erythematous rash on the cheeks, and very slightly on the trunk. The hands and feet were red, enormously swollen, but felt cold to the touch. A few furuncles were to be seen in various parts of the body, and two superficial ulcers on the toes and fingers. There was some desquamation on the fingers and dorsum of the feet. The baby had thirteen teeth, one lower lateral incisor was missing. The tongue showed a superficial ulcer on each side. The reflexes were normal. Tachycardia was marked, the pulse was 160. A few mucous râles were to be heard in both lungs. Blood examination, hemoglobin 100 per cent., red cells, 5,600,000; leukocytes, 21,000; polymorphonuclear cells in excess. Urine normal, Pirquet negative.

Two weeks later a marked improvement in the hands and feet was noticed, but a necrosis began in the lower jaw, involving the site of the lower central incisors and spread to the lips. The teeth came out and also a piece of bone. A semilunar shaped portion of the lower lips separated as a necrotic mass. The skin around the mouth was red, swollen and covered by a thin necrotic epidermis. The left nostril discharged a thin serous pus. The margins of the tongue were necrotic and ulcerated. The blood count remained unchanged. The baby lost weight, refused food and forcible feeding had to be instituted. During the last two weeks marked dysuria and repeated rectal prolapse has become troublesome, but she has ceased losing in weight and the extension of the necrosis has also ceased.

An Epidemic of Erythema Infectiosum. Presented by Dr. John Zahorsky.

Griffith makes the statement that erythema infectiosum has not been observed in English speaking countries. Probably no report is found in the American literature. About ten years ago I had quite a number of cases during a local epidemic; recently, I encountered nine more cases of this disease in an epidemic limited to the western part of the city and immediate suburbs. The classical symptoms are: a scarlet erythema of the cheek, morbilliform rash on the extensor surface of the arms and forearms, maculopapular rash on the gluteal region, rash on the anterior part of the thigh. The rash on the outer part of the arms

had a peculiar tendency to annular grouping. The cervical glands were not enlarged; no catarrhal symptoms and no febrile movement was observed. The disease was distinctly contagious. The fact that at the same period and in the same territory about eleven cases of typical rubella were observed lends support to the theory that this disease is only a spurious or modified form of German measles.

ABSTRACT OF REPORT ON THE HEALTH OF COLORED BABIES IN ST. LOUIS. Presented by DR. PARK J. WHITE.

Total infant death rate, St. Louis, 1923..... 69.2 per cent.
White infant death rate, St. Louis, 1923..... 63.3 per cent.
Colored infant death rate, St. Louis, 1923..... 126.0 per cent.

Poverty and ignorance are the principal causes of the high infant mortality rate. The father's income determines whether or not the family hygiene is what it should be, whether or not the mother is employed, etc. It is inevitable, in St. Louis as elsewhere, that the infant mortality rate is very high.

Total stillborn infants in St. Louis, 1923, 941 (5.82 per cent. of all births).
White stillborn infants in St. Louis, 1923, 714 (4.93 per cent. of white births).
Colored stillborn infants in St. Louis, 1923, 227 (13.26 per cent. of colored births).
Deaths under 1 month, St. Louis, 1923, 517 (3.4 per cent. living births).
White under 1 month, St. Louis, 1923, 427 (3.2 per cent. white births).
Colored under 1 month, St. Louis, 1923, 90 (6.0 per cent. colored births).

Inadequate or improper prenatal and natal care, employment during pregnancy, illegitimacy, venereal diseases, etc., explain these figures.

Accurate illegitimacy rates for St. Louis are not obtainable. Though illegitimacy among the colored is far higher in proportion, colored illegitimate children are so commonly cared for by other families that they are little if any more handicapped than colored legitimate children.

Incidence of Rickets and Malnutrition Among Clinic Babies Between 1 and 2 Years Old When First Seen

	WHITE		COLORED	
	No.	Per Cent.	No.	Per Cent.
Normal	217	65.4	27	31
Malnourished	43	12.8	8	9
Rachitic	49	14.7	30	34
Malnourished and rachitic	24	7.1	23	26
	334		88	

Poverty and ignorance, with resulting poor living quarters, inadequate sunshine, improper feeding, are clearly responsible for the enormously higher incidence of malnutrition and rickets among colored babies.

With regard to hereditary syphilis (Jeans and Cooke), its incidence among colored infants is 15 per cent.; among the poor of the white race 1.8 per cent. (these figures are for St. Louis).

Children's Hospital statistics show that the incidence of positive tuberculin tests among white children of the hospital class in St. Louis has decreased from an average per cent. positive of 39 prior to 1915 to about 8 in 1921 (children of all ages). In 1923-1924 the average per cent. positive in colored children is 34.3, nearly as high as for the whites in 1915 and before, and about four times as high as the more recent figure for white children.

Thus, the colored baby in St. Louis has half the white baby's chance for survival, and from two to three times the white baby's chance for contracting the (largely preventable) diseases mentioned.

As proponents of preventive medicine, it is our imperative duty to give our whole-hearted support to any movement aiming at improved conditions for our colored population.

Book Reviews

TUBERCULOSIS OF THE BONES AND JOINTS. By F. OEHLECKER, Berlin and Vienna, Urban and Schwarzenberg, 1924.

As the author states in the text, this book is written for the purpose of serving as a guide to the practitioner whose judgment is so often hampered and biased by the many publications which one-sidedly advance the benefits of special methods of treatment.

The pathologic section contains a clear and concise description of the tissue changes, as well as a clear discussion of the bacteriologic aspects.

In the diagnoses the clinical syndromes are given due prominence. Tuberculin reaction, as well as the guinea-pig and other diagnostic tests are discussed on the basis of the large personal experience and the keen judgment of the author.

In the discussion of the general treatment heliotherapy is given a large space. The discussion of theories and principles of this type of treatment offers very interesting and instructive reading.

The author also goes at some length into the discussion of the artificial light treatment, especially the Alpine lamp, which he considers of distinct advantage as a substitute for heliotherapy when direct sun treatment is not available.

It is very gratifying to note that the author's views on the surgical treatment of the afflicted joints is thoroughly sound and that he does not permit himself to become biased by any special type of treatment.

Immobilization in plaster of paris is given its due place in the conservative treatment, along with extension and recumbency. The same moderation and conservatism apply in the section on the treatment of cold abscesses and sinuses, and above all to the chapter on the surgical treatment of tuberculosis.

Only intra-osseous foci, easily accessible, are operative indications for removal of the focus. Joint dissections are advised for the adult and condemned for the juvenile patient. For the former, resection is advised for the knee and occasionally for the elbow.

In regard to Bier's hyperemia treatment, the author observes a certain reserve and, for practical value, accords preference to contentive dressings with immobilization.

The roentgen-ray treatment has not given very encouraging results in the opinion of the author. He advises against radiation of growing bones, but he believes that roentgen therapy may be a valuable adjuvant, especially in the case of older patients.

A good deal of space is devoted to the treatment by immunization, with discussion of the different kinds of tuberculins and their different modes of application. Summarizing the results of the specific treatment by tuberculin, the author states that a reasonably reliable specific remedy is at present not available, and that after all the proper general treatment furnishes a better guarantee for systematic immunization of the body.

The special part of the book contains a regional discussion of the clinical pathology of the different bones and joints. Without going in detail into the merits of these chapters, it may be mentioned that they are handled with exceptional clearness and precision, especially with regard to symptomatology and differential diagnosis.

In the matter of treatment, the principles advanced by the author appear to be utterly sound. His conservatism in a discussion of operative methods and their indication, as well as his freedom from partiality for or against any definite surgical method, not always found in modern textbooks, must be of special appeal to the reader.

SÄUGLINGSHEILKUNDE DER TÄGLICHEN PRAXIS. By K. BLÜHDORN, Berlin, Urban and Schwarzenberg, 1924. Fr. 3.75, pp. 190.

This is a short text for general practitioners and medical students. Symptoms, diagnosis and theoretic considerations are given in sufficient detail to explain the therapy but with no attempt at completeness. The subjects are well chosen for their practical importance and are well treated. Such a book has a limited use on account of its brevity.

THE STUDY OF MASTURBATION AND ITS REPUTED SEQUELAE. By JOHN F. W. MEAGHER, M.D., F.A.C.P. Price $1.50, pp. 69. New York, William Wood and Company, N. Y.

This is a small treatise on the subject and should be most interesting to pediatricians. The part this condition plays in child life, is an important one, and the significance of it is well brought out in this short book.

While much of the book is taken up with the condition as it exists in adult life, there are in it many good points for the pediatrician, especially in the treatment.

The author believes that masturbation is practically universal in children, but it is by no means abnormal in young children and that harm is due to excessive indulgence.

The injury is not so much physical, as psychic, and the treatment is along those lines very largely.

Sympathy and encouragement are of much value to the patient.